OM of: US-09-303-518D-649 to: A_Geneseq_032802:* out_format : pfs

Date: Jun 30, 2002 6:48 AM

About: Results were produced by the GenCore software, version 4.5,
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Command line parameters:
-MODEL=frame+_n2p.model -DEV=x1h
-Q=/cgn2_1/USPTO_spool/US09303518/runat_28062002_142712_4291/app_query.fasta_1.23501
-DB=A_Geneseq_032802 -QFMT=fastan -SUFFIX=rag -GAPOP=12.000
-GAPEXT=4.000 -MINMATCH=0.100 -LOOPCL=0.000 -LOOPEXT=0.000
-QGAPOP=4.500 -QGAPEXT=0.050 -XGAPOP=10.000 -XGAPEXT=0.500
-FGAPOP=6.000 -FGAPEXT=7.000 -YGAPOP=10.000 -YGAPEXT=0.500
-DELOP=6.000 -DELEXT=7.000 -START=1 -MATRIX=blosum62
-TRANS=human40.cdi -LIST=100 -DOCALIGN=200 -THR_SCORE=pct
-THR_MAX=100 -THR_MIN=0 -ALIGN=45 -MODE=LOCAL -OUTFMT=pfs
-NORM=ext -HEAPSIZE=500 -MINLEN=0 -MAXLEN=2000000000
-USER=US09303518_@CGN1_1_0 -NCPU=6 -ICPU=3 -LONGLOG
-DEV_TIMEOUT=120 -WARN_TIMEOUT=30 -NO_XLPXY -WAIT -THREADS=1

Search information block:
Query: US-09-303-518D-649
Query length: 4374
Database: A_Geneseq_032802:*
Database sequences: 747574
Database length: 111073796
Search time (sec): 627.340000

score_list:

Sequence	Strd	Orig	ZScore	EScore	Len	! Documentation
/SIDS1/gcgdata/geneseq/geneseqp-embl/AA1990.DAT:AAR07304	+	1608.50	2079.18	7.4e-109	15	
/SIDS1/gcgdata/geneseq/geneseqp-embl/AA2000.DAT:AAY75564	+	1547.00	1999.29	2.2e-104	14	
/SIDS1/gcgdata/geneseq/geneseqp-embl/AA2001.DAT:ABB52745	+	1071.00	1375.04	1.4e-69	13	
/SIDS1/gcgdata/geneseq/geneseqp-embl/AA2001.DAT:ABB52592	+	1053.00	1351.37	2.9e-68	13	
/SIDS1/gcgdata/geneseq/geneseqp-embl/AA1997.DAT:AAW27705	+	715.50	924.55	7.3e-44	32	
/SIDS1/gcgdata/geneseq/geneseqp-embl/AA1988.DAT:AAP80136	+	420.00	527.48	4.1e-22	74	
/SIDS1/gcgdata/geneseq/geneseqp-embl/AA2001.DAT:AAG98842	+	364.50	446.29	6.5e-18	15	
/SIDS1/gcgdata/geneseq/geneseqp-embl/AA2000.DAT:AAB01830	+	307.00	373.61	9.4e-14	12	
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/SIDS1/gcgdata/geneseq/geneseqp-embl/AA1992.DAT:AAR26503	+	297.50	364.41	4.1e-13	91	
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seq_documentation_block:
ID AAR07304 standard; protein; 1541 AA.
XX
AC AAR07304;
XX
DT 31-JAN-1991 (first entry)
XX
DE IgA1 protease.
XX
KW IgA1; vaccine; meningitis; gonnorhoea; allergies.
XX
OS Haemophilus influenzae.
XX
PN WO9011367-A.
XX
PD 04-OCT-1990.
XX
PF 16-MAR-1990; 90WO-DK00073.
XX
PR 17-MAR-1989; 89DK-0001308.
XX

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PA   (KILI/) KILIAN M.
XX
PI   Kilian M,  Poulsen K;
XX
DR   WPI; 1990-320267/42.
DR   N-PSDB; AAQ06164.
XX
PT   Immunoglobulin A1 protease prodn. - by cloning from
PT   microorganisms for immunisation against immunoglobulin A1
PT   protease producing bacteria
XX
PS   Disclosure; fig 3; 44pp; English.
XX
CC   This immunoglobulin (Ig)A1 protease is produced by recombinant DNA
CC   methods.  It is useful in a vaccine for e.g. meningococcal meningitis,
CC   gonorrhoea or allergic diseases.  It specifically cleaves the heavy
CC   chain of human IgA1 in the hinge region.
XX
SQ   Sequence   1541 AA;
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alignment_scores:
            Quality: 1608.50              Length:   1717
              Ratio:  1.733                 Gaps:     51
 Percent Similarity:  54.048   Percent Identity: 27.257

alignment_block:
 US-09-303-518D-649 x AAR07304   ..

 Align seg 1/1  to: AAR07304  from: 1  to: 1541

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         :::|||:::      :::::::|||:::   :::::::::::::::   ||
       5 LysPheLysLeuAsnPheIleAlaLeuThrValAlaTyrAlaLeuThrPr 21

     114 CCAAGCCTGGGCGGGACACACTTATTTCGGCATCAACTACCAATACTATC 163
         |   :::   |||:::   :::         :::::|||||   :::|
      21 oTyrThrGluAlaAlaLeuValArgAspAspValAspTyrGlnIlePheA 38

     164 GCGACTTTGCCGAAAATAAAGGCAAGTTTGCAGTCGGGGCGAAAGATATT 213
         |||||||||||||||||||||||||||:::|||||||||   ::::::
      38 rgAspPheAlaGluAsnLysGlyLysPheSerValGlyAlaThrAsnVal 54

     214 GAGGTTTACAACAAAAAAGGGGAGTTGGTCGGCAAATCAATGACAAAAGC 263
         |||   :::|||:::::::::   :::|||   ::::::   :::::
      55 LeuValLysAspLysAsnAsnLysAspLeuGlyThrAlaLeuProAsnGl 71

     264 C...CCGATGATTGATTTTTCTGTGGTGTCG...CGTAACGGCGTGGCGG 307
         :   |||||||||||||||||||||||:::       :::   :::||:
      71 yIleProMetIleAspPheSerValValAspValAspLysArgIleAlaT 88

     308 CATTGGTGGGCGATCAATATATTGTGAGCGTGGCACAT..... 345
         ::|||::::::   ||||||:::|||:::|||   |||
      88 hrLeuIleAsnProGlnTyrValValGlyValLysHisValSerAsnGly 104

     346 .........................AACGGCGGCTATAACAACGTTGA 368
                                  |||||||:::   ||||||   ::
     105 ValSerGluLeuHisPheGlyAsnLeuAsnGlyAsnMetAsnAsnGlyAs 121

     369 TTTTGGTGCGGAAGGAAGAAATCCCGATCAACATCGTTTTACTTATAAAA 418
         :      |||:::   |||:::   ::::::::::::      |||
     121 nAlaLysAlaHis...ArgAspValSerSerGluGluAsnArgTyrPheS 137

     419 TTGTGAAACGGAATAATTATAAAGCAGGGACTAAAGGC..... 456
           |||:::::::|||:::|||   :::       :::|||
     137 erValGluLysAsnGluTyrProThrLysLeuAsnGlyLysThrValThr 153

     457 ..............CATCCTTATGGCGGCGATTATCATATGCCGCGTTT 491
                         :::                |||||||:::||||||||||
     154 ThrGluAspGlnThrGlnLysArgArgGluAspTyrTyrMetProArgLe 170

     492 GCATAAATTTGTCACAGATGCAGAACCTGTTGAA...ATGACCAGTTATA 538
         |   ||||||||||||:::::   |||:::|||      |||:::
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     170 uAspLysPheValThrGluValAlaProIleGluAlaSerThrAlaSerS 187

     539 TGGATGGGCGGAAATATATCGATCAAAATAATTACCCTGACCGTGTTCGT 588
           |||:::      |||   |||||||||:::|||||      ||||||
     187 erAspAlaGlyThrTyrAsnAspGlnAsnLysTyrProAlaPheValArg 203

     589 ATTGGGGCAGGCAGGCAATATTGGCGATCTGATGAAGATGAG..... 630
         :::|||:::|||   |||:::      :::      |||:::
     204 LeuGlySerGlySerGlnPheIleTyrLysLysGlyAspAsnTyrSerLe 220

     631 ....CCCAATAACCGCGAAAGTTCATATCAT.....ATTGCAA 664
               ||||||:::|||   :::   :::           :::::::
     220 uIleLeuAsnAsnHisGluValGlyGlyAsnAsnLeuLysLeuValGlyA 237

     665 GTGCGTATTCTTGGCTCGTTGGTGGCAATACCTTTGCACAAAATGGATCA 714
         ::||||||:::::   :::::::|||:::   :::      |||   :::
     237 spAlaTyrThrTyrGlyIleAlaGlyThrProTyrLysValAsnHisGlu 253

     715 GGTGGTGGCACAGTCAACTTAGGTAGTGAAAAAATTAAACATAGC...CC 761
         ::::::|||   :::::::::|||:::::::|||   :::||||||   ||
     254 AsnAsnGlyLeuIleGlyPheGlyAsnSerLysGluGluHisSerAspPr 270

     762 ATATGGTTTTTTACCAACAGGA.............GGCTCATTTGGCG 796
         |   |||:::|||                      :::   :::|||||
     270 oLysGlyIleLeuSerGlnAspProLeuThrAsnTyrAlaValLeuGlyA 287

     797 ACAGTGGCTCACCAATGTTTATCTATGATGCCCAAAAGCAAAAGTGGTTA 846
         ||||||||||||||:::|||:::||||||   :::|||   |||||||||
     287 spSerGlySerProLeuPheValTyrAspArgGluLysGlyLysTrpLeu 303

     847 ATTAATGGGGTATTGCAAACGGGCAACCCCTATATAGGAAAAAGCAATGG 896
         :::   |||      :::            |||      ||||||
     304 PheLeuGlySerTyrAspPheTrpAlaGlyTyrAsnLysLysSer..... 318

     897 CTTCCAGCTGGTTCGTAAAGATTGG...TTCTATGATGAAATCTTTGCTG 943
                        :::::::|||   :::|||   :::   |||:::
     319 .............TrpGlnGluTrpAsnIleTyrLysSerGlnPheThrL 331

     944 GAGATACCCATTCAGTATTCTACGAACCACGTCAAAATGGGAAATACTCT 993
           |||:::
     331 ysAspVal..................................... 333

     994 TTTAACGACGATAATAATGGCACAGGAAAAATCAATGCCAAACATGAACA 1043
         :::|||   |||:::   |||:::      |||::::::|||   :::::
     334 LeuAsnLysAspSerAlaGlySer...LeuIleGlySerLysThrAspTy 349

    1044 CAATTCTCTGCCTAATAGATTAAAAACACGAACCGTT.....C 1081
         ::::         |||      ||||||   |||:::         :
     349 rSerTrpSerSerAsnGly...LysThrSerThrIleThrGlyGlyGluL 365

    1082 AATTGTTTAATGTTTCTTTATCCGAGACAGCAAGAGAACCTGTTTATCAT 1131
         ::   :::|||||||:::|||:::::::      :::|||
     365 ysSerLeuAsnValAspLeuAlaAspGlyLysAspLysPro..... 378

    1132 GCTGCAGGTGGTGTCAACAGTTATCGACCCAGACTGAATAATGGAGAAAA 1181
                                                |||:::|||:::::
     379 ..................................AsnHisGlyLysSe 383

    1182 TATTTCCTTTATTGACGAAGGAAAAGGCGAATTGATACTTACCAGCAACA 1231
         ::::::::|||      ||||||:::|||   |||   |||:::::::||||
     383 rValThrPhe......GluGlySerGlyThrLeuThrLeuAsnAsnAsnI 398

    1232 TCAATCAAGGTGCTGGAGGATTATATTTCCAAGGAGATTTTACGGTC... 1278
         ||:::|||||||||||||||||||:::|||:::|||||||:::   |||
     398 leAspGlnGlyAlaGlyGlyLeuPhePheGluGlyAspTyrGluValLys 414

    1279 TCGCCTGAAAATAACGAAACTTGGCAAGGCGCGGGCGTTCATATCAGTGA 1328
         :::   :::::::|||   ||||||:::|||||||||||||   :::::::||
     415 GlyThrSerAspAsnThrThrTrpLysGlyAlaGlyValSerValAlaGl 431

    1329 AGACAGTACCGTTACTTGGAAAGTAAACGGCGTGGCAAACGACCGCCTGT 1378
         |   :::|||||||||||||||||||:::::         |||||||||:
     431 uGlyLysThrValThrTrpLysValHisAsnProGlnTyrAspArgLeuA 448
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1379 CCAAAATCGGCAAAGGCACGCTGCACGTTCAAGCCAAAGGGGAAAACCAA 1428
     ::|||||||||||||||||||||   |||:::::::   |||:::|||:::
 448 laLysIleGlyLysGlyThrLeuIleValGluGlyThrGlyAspAsnLys 464

1429 GGCTCGATCAGCGTGGGCGACGGTACAGTCATTTTGGATCAGCAGGCAGA 1478
     ||||||:::::|||||||||||||||||||||||||   ||||||:::::
 465 GlySerLeuLysValGlyAspGlyThrValIleLeuLysGlnGlnThrAs 481

1479 CGATAAAGGCAAAAAACAAGCCTTTAGTGAAATCGGCTTGGTCAGCGGCA 1528
     :   :::|||   ::::::||||||:::::::::|||:::||||||||||
 481 nGlySerGly...GlnHisAlaPheAlaSerValGlyIleValSerGlyA 497

1529 GGGGTACGGTGCAACTGAATGCCGATAATCAGTTCAACCCCGACAAACTC 1578
     ||:::|||:::   ||||||   |||:::|||   :::|||:::::::::
 497 rgSerThrLeuValLeuAsnAspAspLysGlnValAspProAsnSerIle 513

1579 TATTTCGGCTTTCGCGGCGGACGTTTGGATTTAAACGGGCATTCGCTTTC 1628
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1713 ..... 1713

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1713 ..... 1713

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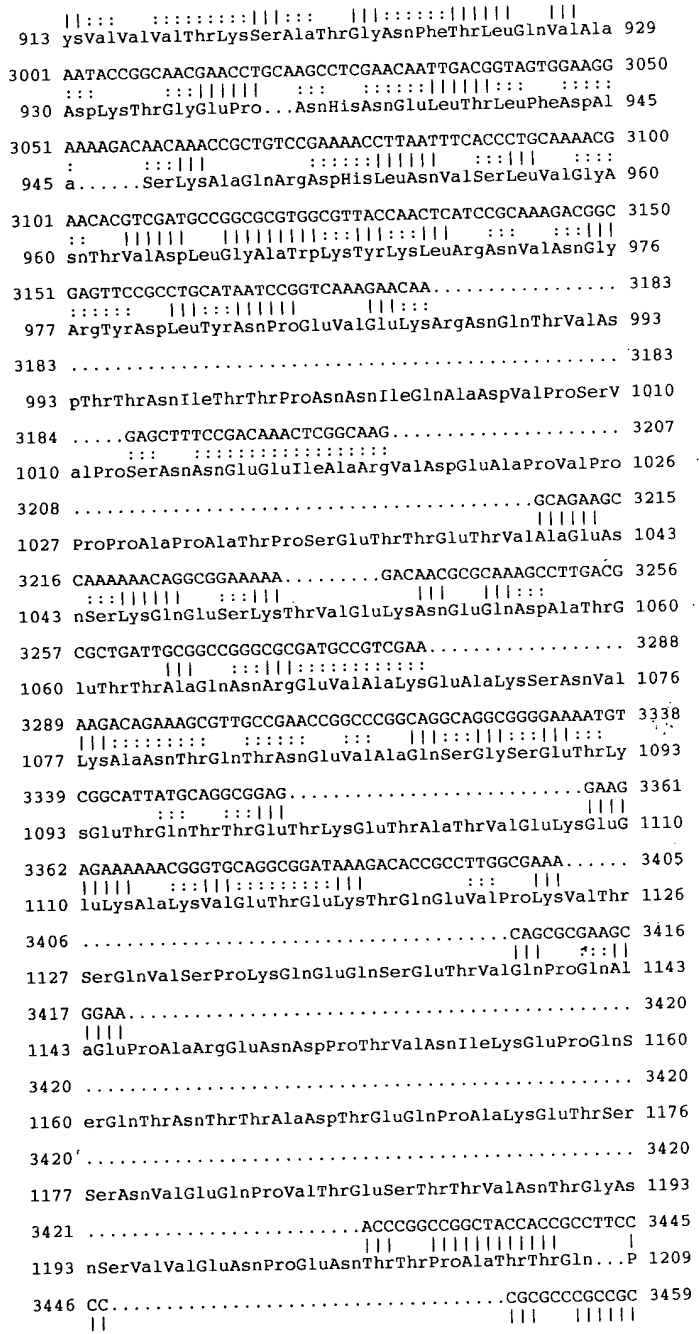
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PR   02-SEP-1998;   98US-0098994.
PR   02-SEP-1998;   98US-0099062.
PR   09-OCT-1998;   98US-0103749.
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DR   WPI; 2000-062150/05.
DR   N-PSDB; AAZ54326.
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PT   Novel Neisserial polypeptides predicted to be useful antigens for
PT   vaccines and diagnostics  -
XX
PS   Claim 2; Page 1234; 1453pp; English.
XX
CC   AAZ53015 to AAZ54536, AAZ54577 to AAZ54615, and AAY74253 to AAY75941
CC   represent novel Neisseria meningitis and N. gonorrheae polynucleotides
CC   and polypeptides. AAZ54537 to AAZ54576 and AAZ54616 to AAZ55473 represent
CC   PCR primers used in the exemplification of the present invention. The
CC   polypeptides, the polynucleotides, antibodies and compositions of
CC   the invention can be used as vaccines, as diagnostic reagents, and as
CC   immunogenic compositions. The polypeptides can be used in the
CC   manufacture of medicaments for treating or preventing infection due to
CC   Neisserial bacteria (e.g. meningitis and septicaemia), to detect the
CC   presence of Neisseria bacteria, or to raise antibodies. They may also
CC   be used to screen for agonists or antagonists, which may themselves
CC   have use as antibacterial agents. The polynucleotides of the invention
CC   may also be used in gene therapy protocols.
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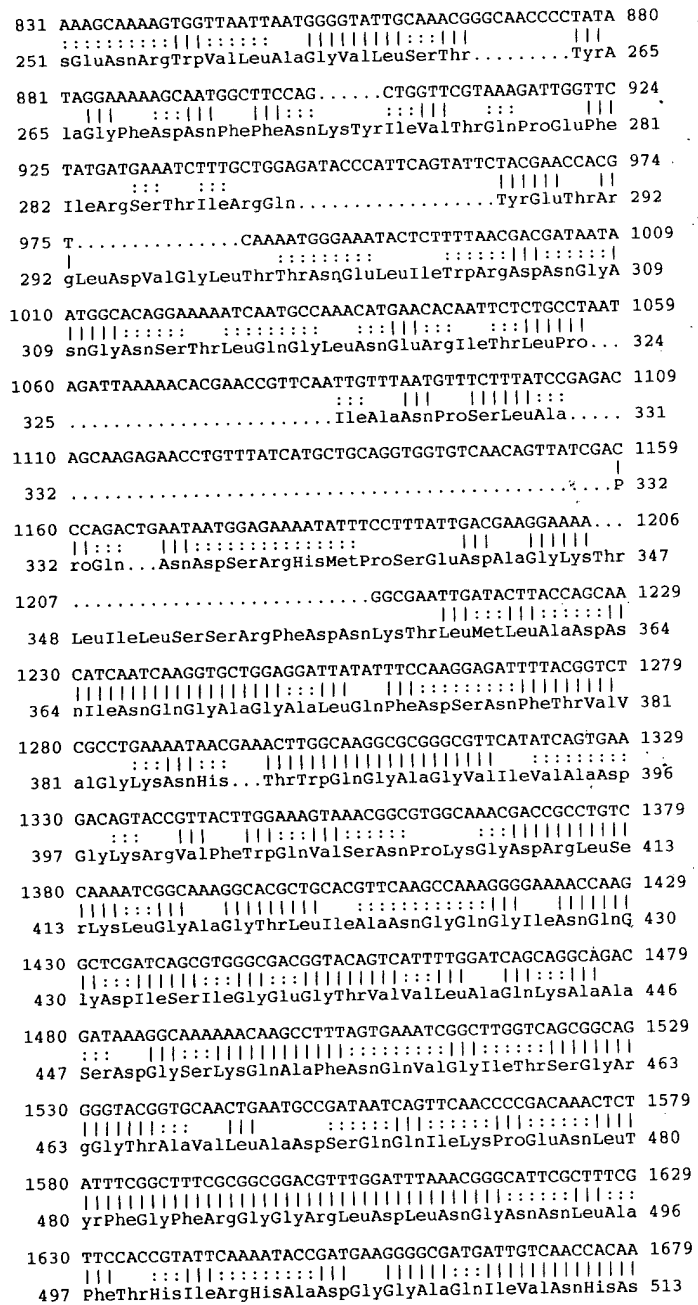

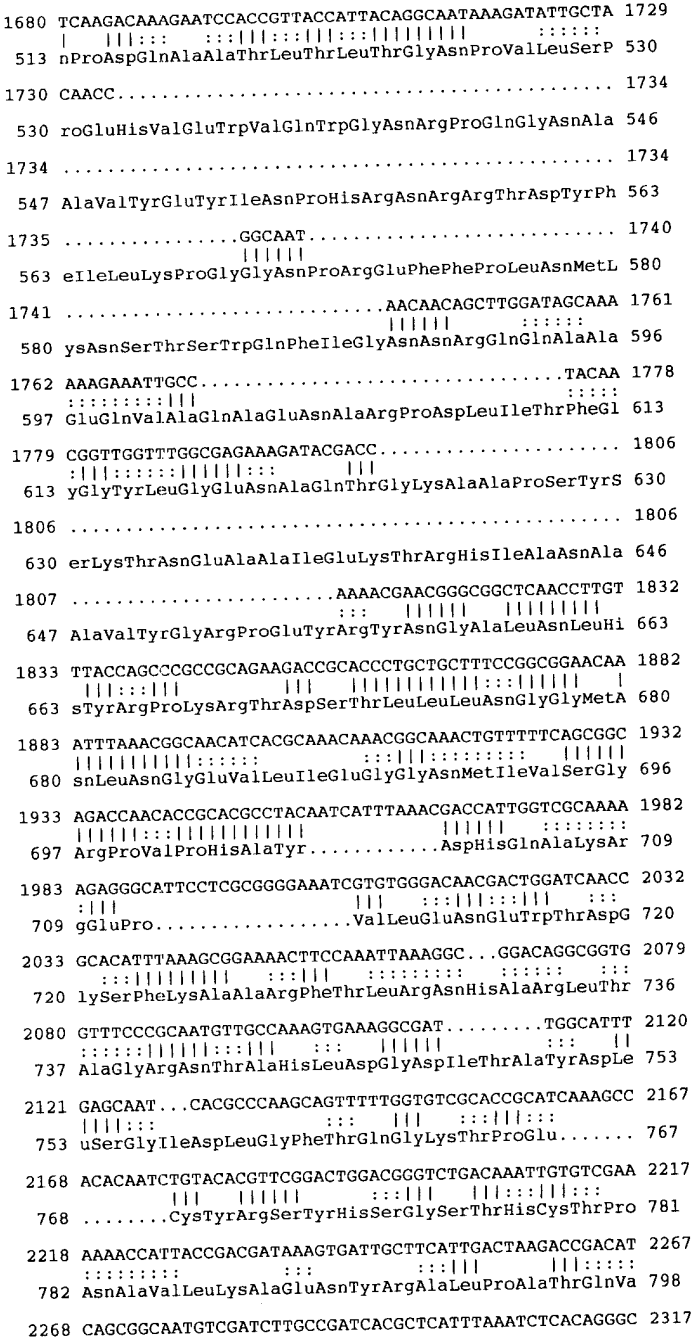

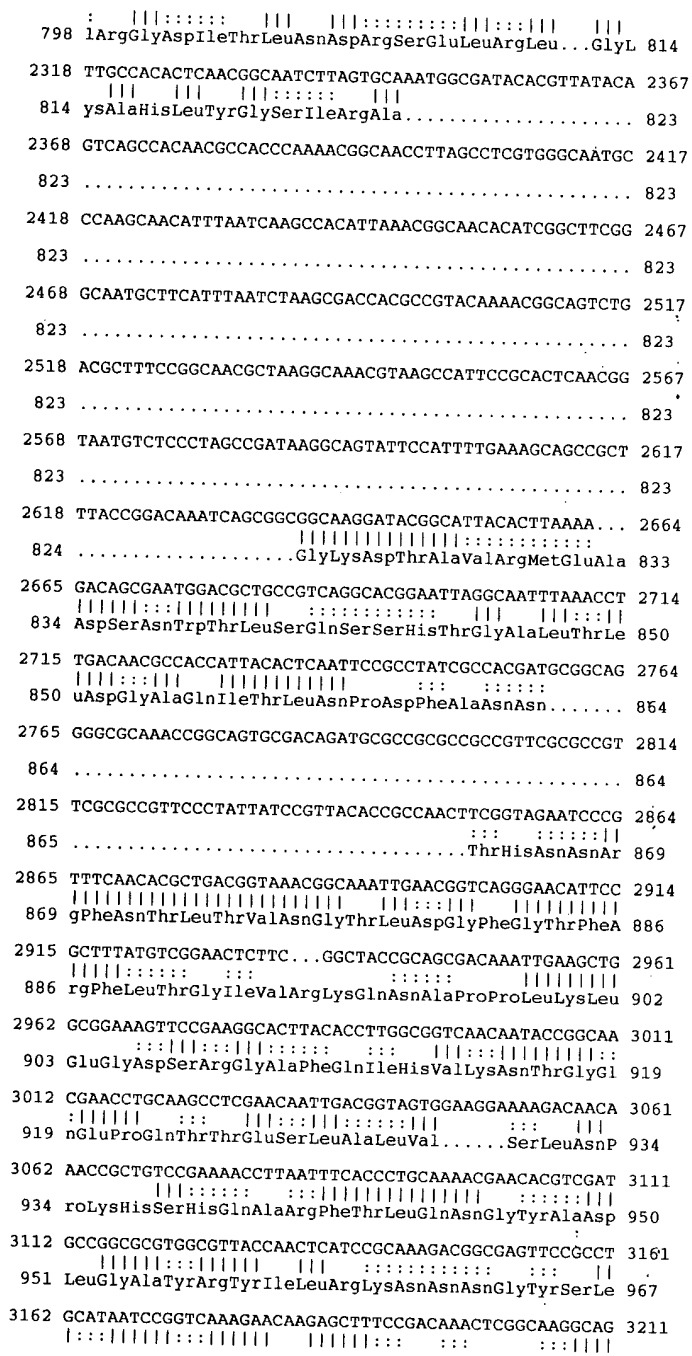
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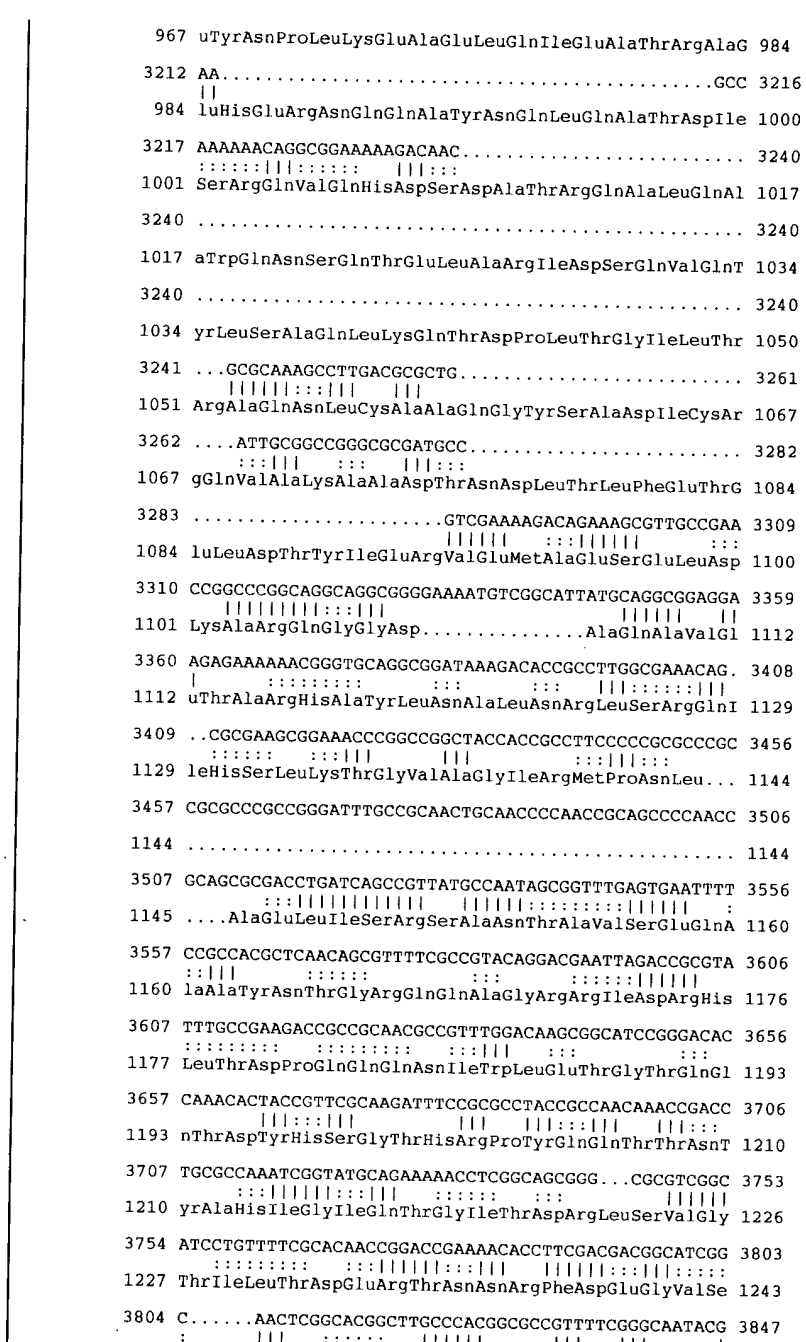
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3212 AA.....GCC 3216
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3217 AAAAAACAGGCGGAAAAAGACAAC..... 3240
1001 SerArgGlnValGlnHisAspSerAspAlaThrArgGlnAlaLeuGlnAl 1017
3240 3240
1017 aTrpGlnAsnSerGlnThrGluLeuAlaArgIleAspSerGlnValGlnT 1034
3240 3240
1034 yrLeuSerAlaGlnLeuLysGlnThrAspProLeuThrGlyIleLeuThr 1050
3241 ...GCGCAAAGCCTTGACGCGCTG..... 3261
1051 ArgAlaGlnAsnLeuCysAlaAlaGlnGlyTyrSerAlaAspIleCysAr 1067
3262 ....ATTGCGGCCGGGCGCGATGCC..... 3282
1067 gGlnValAlaLysAlaAlaAspThrAsnAspLeuThrLeuPheGluThrG 1084
3283 .....GTCGAAAAGACAGAAAGCGTTGCCGAA 3309
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1101 LysAlaArgGlnGlyGlyAsp.....AlaGlnAlaValGl 1112
3360 AGAGAAAAAACGGGTGCAGGCGGATAAAGACACCGCCTTGGCGAAACAG. 3408
1112 uThrAlaArgHisAlaTyrLeuAsnAlaLeuAsnArgLeuSerArgGlnI 1129
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1129 leHisSerLeuLysThrGlyValAlaGlyIleArgMetProAsnLeu... 1144
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1144 1144
3507 GCAGCGCGACCTGATCAGCCGTTATGCCAATAGCGGTTTGAGTGAATTTT 3556
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3557 CCGCCACGCTCAACAGCGTTTTCGCCGTACAGGACGAATTAGACCGCGTA 3606
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3607 TTTGCCGAAGACCGCCGCAACGCCGTTTGGACAAGCGGCATCCGGGACAC 3656
1177 LeuThrAspProGlnGlnGlnAsnIleTrpLeuGluThrGlyThrGlnGl 1193
3657 CAAACACTACCGTTCGCAAGATTTCCGCGCCTACCGCCAACAAACCGACC 3706
1193 nThrAspTyrHisSerGlyThrHisArgProTyrGlnGlnThrThrAsnT 1210
3707 TGCGCCAAATCGGTATGCAGAAAAACCTCGGCAGCGGG...CGCGTCGGC 3753
1210 yrAlaHisIleGlyIleGlnThrGlyIleThrAspArgLeuSerValGly 1226
3754 ATCCTGTTTTCGCACAACCGGACCGAAAACACCTTCGACGACGGCATCGG 3803
1227 ThrIleLeuThrAspGluArgThrAsnAsnArgPheAspGluGlyValSe 1243
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  1273 SerArgThrArgPheThrAspTyrAspGlyAlaAlaValArgArgHisAl 1289

  3942 GCTGCATTACGGCATTCAGGCACGATACCGCGCCGGTTTCGGCGGATTCG 3991
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  1289 aTrpAspAlaGlyIleAsnThrGlyIleLysIleAsp...ThrGlyIleA 1305

  3992 GCATCGAACCGCACATCGGC.....................GCAACGCGC 4020
       ::::::::|||:::   |||                     ::::::||| 
  1305 snLeuArgProTyrAlaGlyIleArgIleAsnArgSerAsnGlyAsnArg 1321

  4021 TATTTCGTCCAAAAAGCGGATTACCGCTACGAAAACGTCAATATCGCCAC 4070
       |||   ::::::   |||:::                    |||   ::  
  1322 TyrValLeuAspGlyAlaGlu.....................IleAsnSe 1331

  4071 CCCCGGCCTTGCATTCAACCGCTACCGCGCGGGCATTAAGGCAGATTATT 4120
       :|||:::        :::   ::::::|||||||||:::   |||   :
  1331 rProAlaGlnIleGlnThrThrTrpHisAlaGlyIleArgLeuAspLysT 1348

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  1379 pArgThrLeuLeuGlnGlnAlaAlaHisGlyThrLeuHisThrLeuGlnI 1396

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  4315 AAAGGCCCGCAACTGGAAGCGCAACACAGCGCGGGCATCAAATTAGGCTA 4364
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seq_documentation_block:

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AC   ABB52745;
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DT   11-FEB-2002  (first entry)
XX
DE   Escherichia coli polypeptide SEQ ID NO 891.
XX
KW   Escherichia coli; B2/D+A-; antiinflammatory; antibacterial;
KW   immunosuppressive; extra-intestinal infection; phylogeny; meningitis;
KW   systemic infection; non-diarrhoeal infection; septicaemia;
KW   pyelonephritis; antibiotic resistance.
XX
OS   Escherichia coli.
XX
PN   WO200166572-A2.
XX
PD   13-SEP-2001.
XX
PF   12-MAR-2001; 2001WO-EP03445.
XX
PR   10-MAR-2000; 2000FR-0003145.
PR   02-FEB-2001; 2001FR-0001449.
XX
PA   (INRM ) INSERM INST NAT SANTE & RECH MEDICALE.
XX
PI   Bingen E,  Bonacorsi S,  Clermont O,  Nassif X,  Tinsley C;
XX
DR   WPI; 2001-550253/61.
XX
PT   A library of DNA fragments of Escherichia coli strains for the
PT   phylogenic determination of a given strain comprises polynucleotides of
PT   nature B2/D+ A- -
XX
PS   Example 6; Fig 6; 646pp; English.
XX
CC   The invention relates to a library of DNA fragments of Escherichia coli
CC   strains comprising polynucleotides (ABA88577-ABA88729 and ABA89533)
CC   and encoded proteins (ABB52459-ABB52919 and ABB52954-ABB53094) of nature
CC   B2/D+A-. The polynucleotides have potential antiinflammatory,
CC   antibacterial and immunosuppressive activity as part of pharmaceutical
CC   compositions used to treat, palliate or prevent extra-intestinal E. coli
CC   infections. The polypeptides are useful for determining the phylogenic
CC   group of a given E. coli strain. These polypeptides can detect and treat
CC   an undesired development of E. coli, particularly an extra-intestinal
CC   infection that include systemic and non-diarrhoeal infections such as
CC   septicaemia, pyelonephritis and meningitis this is particularly
CC   advantageous as bacterial resistance is increasing with the more
CC   frequent use of broad spectrum antibiotics.
XX
SQ   Sequence   1371 AA;
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alignment_scores:

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 Percent Similarity:  50.354   Percent Identity: 25.821
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alignment_block:

US-09-303-518D-649 x ABB52745 ..

Align seg 1/1 to: ABB52745 from: 1 to: 1371

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   159 CTATCGCGACTTTGCCGAAAATAAAGGCAAGTTTGCAGTCGGGGCGAAAG 208
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    66 eTyrArgAspPheAlaGluAsnLysGlyLeuPheValProGlyAlaThrA 83

   209 ATATTGAGGTTTACAACAAAAAAGGGGAGTTGGTCGGCAAATCAATGACA 258
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    83 spIleProValTyrAspLysAspGlyLysLeuValGlyArg...LeuAsp 98

   259 AAAGCCCCGATGATTGATTTTTCTGTGGTGTCGCGTAACGGCGTGGCGGC 308
       ||||||||||||   |||||||||   ||||||   ||||||||||||:: 
    99 LysAlaProMetAlaAspPheSerSerValSerSerAsnGlyValAlaTh 115

   309 ATTGGTGGGCGATCAATATATTGTGAGCGTGGCACATAACGGCGGCTATA 358
       :||||||:::   ||||||||||||||||||   ||||||||||||||: 
   115 rLeuValSerProGlnTyrIleValSerValLysHisAsnGlyGlyTyrG 132

   359 ACAACGTTGATTTTGGTGCGGAAGGAAGAAATCCCGATCAACATCGTTTT 408
       :::::|||:::||||||   :::|||:::|||                  
   132 lnSerValSerPheGly...AsnGlyLysAsn..................  141

   409 ACTTATAAAATTGTGAAACGGAATAATTATAAAGCAGGGACTAAAGGCCA 458
       ||||||::::::|||   |||||||||:::::::::              
   142 ThrTyrSerLeuValAspArgAsnAsnHisSerSer.............  153

   459 TCCTTATGGCGGCGATTATCATATGCCGCGTTTGCATAAATTTGTCACAG 508
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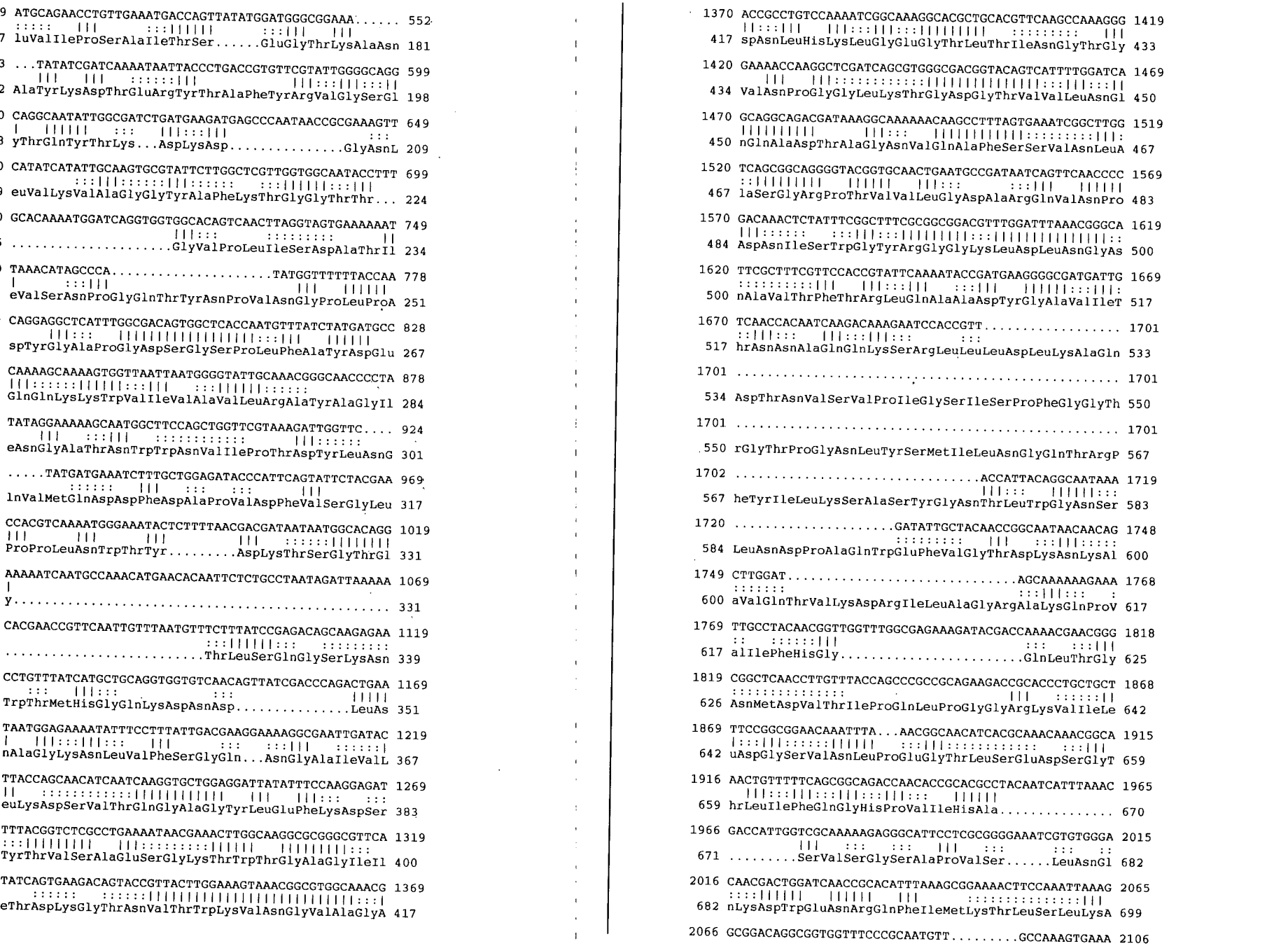

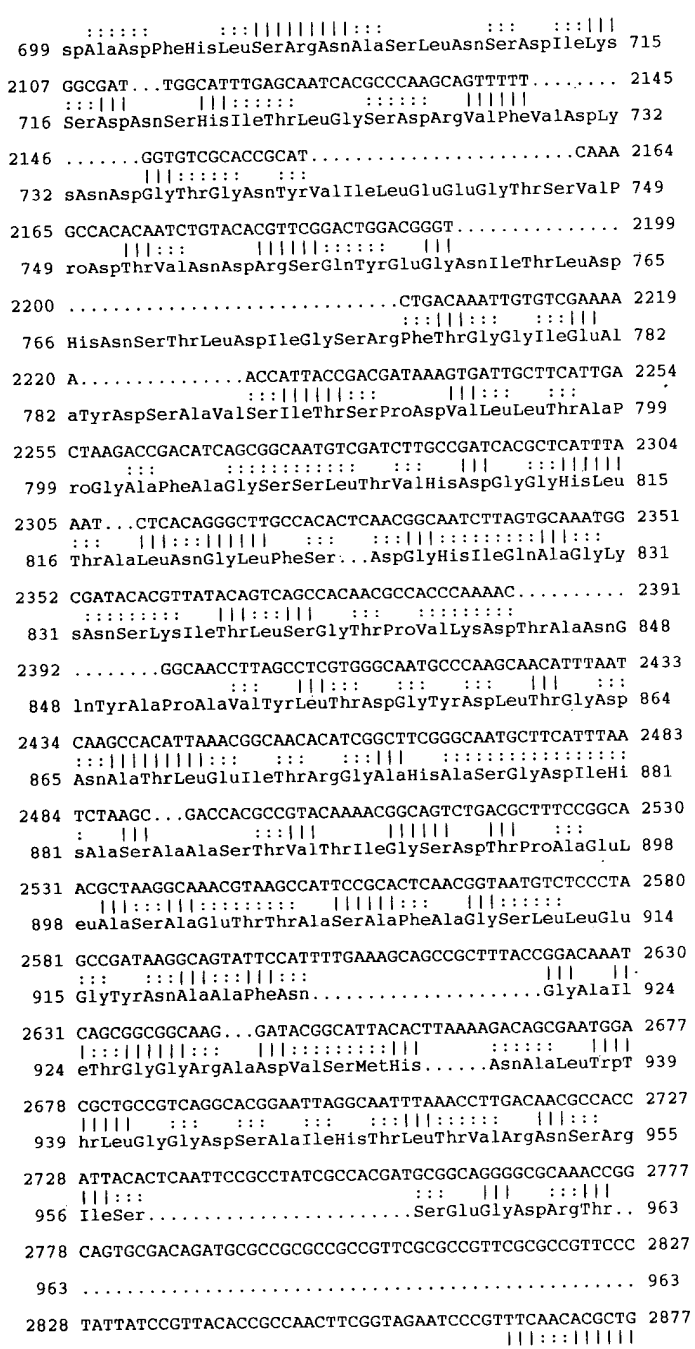
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716 SerAspAsnSerHisIleThrLeuGlySerAspArgValPheValAspLy 732
2146 .....GGTGTCGCACCGCAT.....CAAA 2164
732 sAsnAspGlyThrGlyAsnTyrValIleLeuGluGluGlyThrSerValP 749
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749 roAspThrValAsnAspArgSerGlnTyrGluGlyAsnIleThrLeuAsp 765
2200 .....CTGACAAATTGTGTCGAAAA 2219
766 HisAsnSerThrLeuAspIleGlySerArgPheThrGlyGlyIleGluAl 782
2220 A.....ACCATTACCGACGATAAAGTGATTGCTTCATTGA 2254
782 aTyrAspSerAlaValSerIleThrSerProAspValLeuLeuThrAlaP 799
2255 CTAAGACCGACATCAGCGGCAATGTCGATCTTGCCGATCACGCTCATTTA 2304
799 roGlyAlaPheAlaGlySerSerLeuThrValHisAspGlyGlyHisLeu 815
2305 AAT...CTCACAGGGCTTGCCACACTCAACGGCAATCTTAGTGCAAATGG 2351
816 ThrAlaLeuAsnGlyLeuPheSer...AspGlyHisIleGlnAlaGlyLy 831
2352 CGATACACGTTATACAGTCAGCCACAACGCCACCCAAAAC..... 2391
831 sAsnSerLysIleThrLeuSerGlyThrProValLysAspThrAlaAsnG 848
2392 .....GGCAACCTTAGCCTCGTGGGCAATGCCCAAGCAACATTTAAT 2433
848 lnTyrAlaProAlaValTyrLeuThrAspGlyTyrAspLeuThrGlyAsp 864
2434 CAAGCCACATTAAACGGCAACACATCGGCTTCGGGCAATGCTTCATTTAA 2483
865 AsnAlaThrLeuGluIleThrArgGlyAlaHisAlaSerGlyAspIleHi 881
2484 TCTAAGC...GACCACGCCGTACAAAACGGCAGTCTGACGCTTTCCGGCA 2530
881 sAlaSerAlaAlaSerThrValThrIleGlySerAspThrProAlaGluL 898
2531 ACGCTAAGGCAAACGTAAGCCATTCCGCACTCAACGGTAATGTCTCCCTA 2580
898 euAlaSerAlaGluThrThrAlaSerAlaPheAlaGlySerLeuLeuGlu 914
2581 GCCGATAAGGCAGTATTCCATTTTGAAAGCAGCCGCTTTACCGGACAAAT 2630
915 GlyTyrAsnAlaAlaPheAsn.....GlyAlaIl 924
2631 CAGCGGCGGCAAG...GATACGGCATTACACTTAAAAGACAGCGAATGGA 2677
924 eThrGlyGlyArgAlaAspValSerMetHis.....AsnAlaLeuTrpT 939
2678 CGCTGCCGTCAGGCACGGAATTAGGCAATTTAAACCTTGACAACGCCACC 2727
939 hrLeuGlyGlyAspSerAlaIleHisThrLeuThrValArgAsnSerArg 955
2728 ATTACACTCAATTCCGCCTATCGCCACGATGCGGCAGGGGCGCAAACCGG 2777
956 IleSer.....SerGluGlyAspArgThr.. 963
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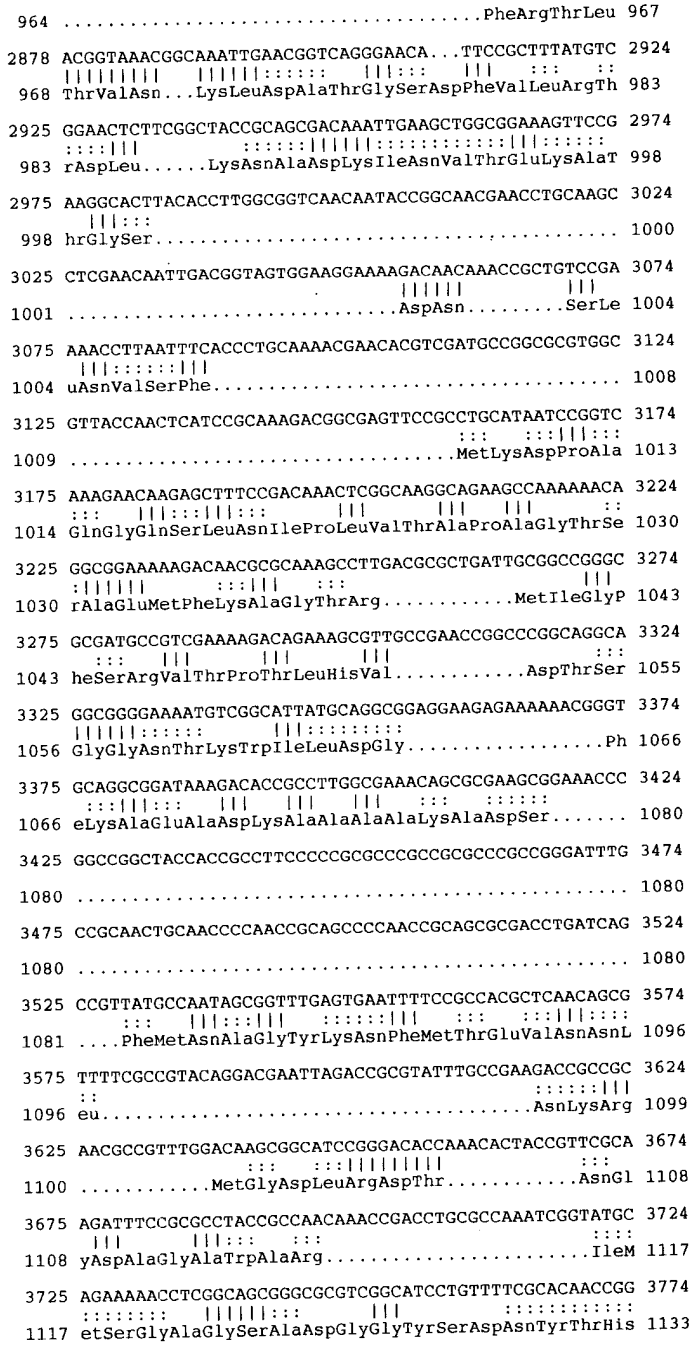
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983 rAspLeu.....LysAsnAlaAspLysIleAsnValThrGluLysAlaT 998
2975 AAGGCACTTACACCTTGGCGGTCAACAATACCGGCAACGAACCTGCAAGC 3024
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3125 GTTACCAACTCATCCGCAAAGACGGCGAGTTCCGCCTGCATAATCCGGTC 3174
1009 .....MetLysAspProAla 1013
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1080 1080
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3575 TTTTCGCCGTACAGGACGAATTAGACCGCGTATTTGCCGAAGACCGCCGC 3624
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1108 yAspAlaGlyAlaTrpAlaArg.....IleM 1117
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 1177 ......GlyLeuTyrAlaSerAlaLeuPheGluSerGlyAlaTyrIleAs 1191

 3912 CGGCATCGGAGGCAAAATCCGCCGCCGCGTGCTGCATTACGGCATTCAGG 3961
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DE   Escherichia coli polypeptide SEQ ID NO 560.
XX
KW   Escherichia coli; B2/D+A-; antiinflammatory; antibacterial;
KW   immunosuppressive; extra-intestinal infection; phylogeny; meningitis;
KW   systemic infection; non-diarrhoeal infection; septicaemia;
KW   pyelonephritis; antibiotic resistance.
XX
OS   Escherichia coli.
XX
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XX
PR   10-MAR-2000; 2000FR-0003145.
PR   02-FEB-2001; 2001FR-0001449.
XX
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XX
PI   Bingen E,  Bonacorsi S,  Clermont O,  Nassif X,  Tinsley C;
XX
DR   WPI; 2001-550253/61.
XX
PT   A library of DNA fragments of Escherichia coli strains for the
PT   phylogenic determination of a given strain comprises polynucleotides of
PT   nature B2/D+ A- -
XX
PS   Example 6; Fig 6; 646pp; English.
XX
CC   The invention relates to a library of DNA fragments of Escherichia coli
CC   strains comprising polynucleotides (ABA88577-ABA88729 and ABA89533)
CC   and encoded proteins (ABB52459-ABB52919 and ABB52954-ABB53094) of nature
CC   B2/D+A-. The polynucleotides have potential antiinflammatory,
CC   antibacterial and immunosuppressive activity as part of pharmaceutical
CC   compositions used to treat, palliate or prevent extra-intestinal E. coli
CC   infections. The polypeptides are useful for determining the phylogenic
CC   group of a given E. coli strain. These polypeptides can detect and treat
CC   an undesired development of E. coli, particularly an extra-intestinal
CC   infection that include systemic and non-diarrhoeal infections such as
CC   septicaemia, pyelonephritis and meningitis this is particularly
CC   advantageous as bacterial resistance is increasing with the more
CC   frequent use of broad spectrum antibiotics.
XX
SQ   Sequence   1376 AA;
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alignment_scores:

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US-09-303-518D-649 x ABB52592 ..

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   80 yAlaThrAsnIleProIlePheAsnAsnLysGlyGluLeuValGly...H 96

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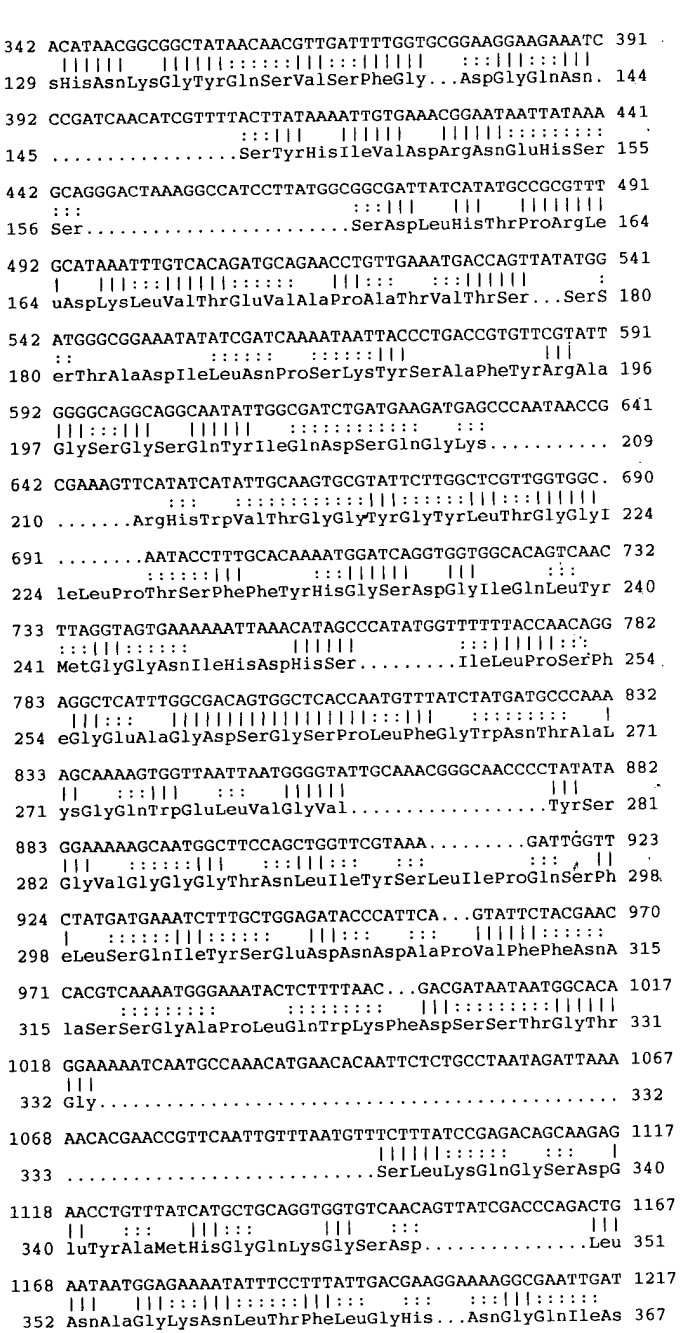

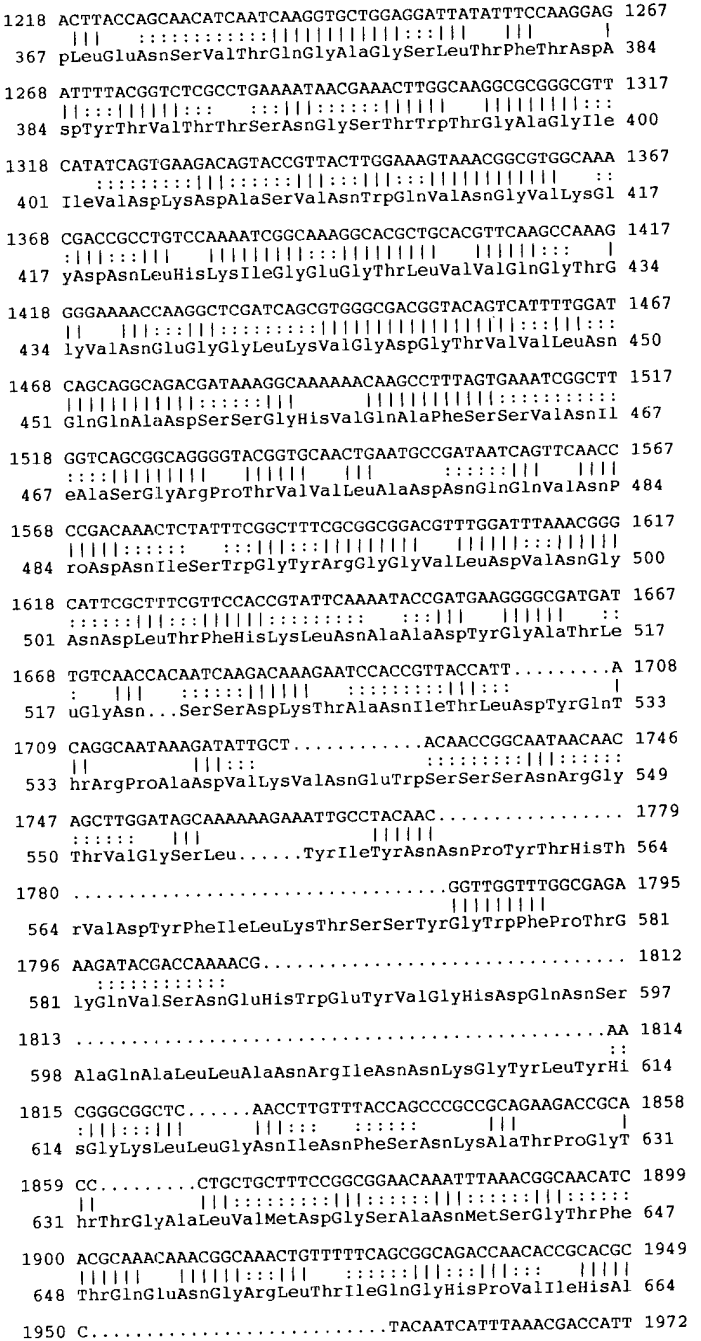

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1973 GGTCGCAAAAAGAGGGCATTCCTCGCGGGGAAATCGTGTGGGACAACGAC 2022
 681 ..........SerValLeuThrGlnProThrSerPheThrGlnAspAsp 693

2023 TGGATCAACCGCACATTTAAAGCGGAAAACTTCCAAATTAAAGGCGGACA 2072
 694 TrpGluAsnArgThrPheSerPheGlySerLeuValLeuLysAspThrAs 710

2073 GGCGGTGGTTTCCCGCAATGTTGCCAAAGTGAAAGGCGATTGGCATTTGA 2122
 710 pPheGlyLeuGlyArgAsnAlaThr.....LeuA 720

2123 GCAATCACGCCCAAGCA...GTTTTTGGTGTCGCACCGCATCAAAGCCAC 2169
 720 snThrThrIleGlnAlaAspAsnSerSerValThrLeuGlyAspSerArg 736

2170 ACAATCTGTACACGTTCGGACTGGACGGGTCTGACAAATTGTGTCGAAAA 2219
 737 ValPheIleAspLysLysAspGlyGlnGlyThrAlaPheThrLeuGluGl 753

2220 A.........ACCATTACCGACGATAAAGTGATTGCTTCATTGACTAAGA 2260
 753 uGlyThrSerValAlaThrLysAsp.............AlaAspLysS 765

2261 CCGACATCAGCGGCAATGTCGATCTTGCCGATCACGCTCATTTAAATCTC 2310
 765 erValPheAsnGlyThrValAsnLeuAspAsnGlnSerValLeuAsnIle 781

2311 ACAGGGCTTGCCACACTCAACGGCAATCTTAGTGCAAATGGCGATACACG 2360
 782 AsnGluIle......PheAsnGlyGlyIleGlnAlaAsnAsnSerThrVa 796

2361 TTATACAGTCAGCCACAACGCCACCCAAAACGGCAACCTTAGCCTCGTGG 2410
 796 lAsnIleSerSerAspSerAla.....ValLeuG 806

2411 GCAATGCCCAAGCAACATTTAATCAAGCCACATTAAACGGCAACACATCG 2460
 806 luAsnSerThrLeuThrSerThrAlaLeuAsnLeuAsnLysGlyAlaAsn 822

2461 GCTTCGGGCAATGCTTCATTT.....AATCTAAGCGA 2492
 823 ValLeuAlaSerGlnSerPheValSerAspGlyProValAsnIleSerAs 839

2493 CCACGCCGTACAA..... 2505
 839 pAlaThrLeuSerLeuAsnSerArgProAspGluValSerHisThrLeuL 856

2506 .....AACGGCAGTCTGACGCTTTCCGGC...AACGCT 2535
 856 euProValTyrAspTyrAlaGlySerTrpAsnLeuLysGlyAspAspAla 872

2536 AAGGCAAACGTAAGC...CATTCCGCACTCAACGGTAATGTCTCCCTAGC 2582
 873 ArgLeuAsnValGlyProTyrSerMetLeuSerGlyAsnIleAsnValGl 889

2583 CGATAAG..... 2589
 889 nAspLysGlyThrValThrLeuGlyGlyGluGlyGluLeuSerProAspL 906

2590 .....GCAGTATTCCATTTTGAAAGCAGC 2613
 906 euThrLeuGlnAsnGlnMetLeuTyrSerLeuPheAsnGlyTyrArgAsn 922

2614 CGCTTTACCGGACAAATCAGCGGCGGCAAGGATACGGCATTACACTTAAA 2663
 923 ThrTrpSerGlySerLeuAsn...AlaProAspAlaThrValSerMetTh 938

2664 AGACAGCGAATGGACGCTGCCGTCAGGCACGGAATTAGGCAATTTAAACC 2713
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 938 rAspThrGlnTrpSerMetAsnGlyAsnSerThrAlaGlyAsnMetLysL 955

2714 TTGACAACGCCACCATTACACTCAATTCCGCCTATCGCCACGATGCGGCA 2763
 955 euAsnArgThrIleValGlyPheAsnGlyGly..... 965

2764 GGGGCGCAAACCGGCAGTGCGACAGATGCGCCGCGCCGCCGTTCGCGCCG 2813
 965 ..... 965

2814 TTCGCGCCGTTCCCTATTATCCGTTACACCGCCAACTTCGGTAGAATCCC 2863
 966 .....ThrSerS 968

2864 GTTTCAACACGCTGACGGTAAACGGCAAATTGAACGGTCAGGGAACATTC 2913
 968 erPheThrThrLeuThrThrAspAsnLeuAspAlaValGlnSerAlaPhe 984

2914 CGCTTTATGTCGGAACTCTTCGGCTACCGCAGCGACAAATTGAAGCTGGC 2963
 985 ValMetArgThrAspLeu......AsnLysAlaAspLysLeuValIleAs 999

2964 GGAAAGTTCCGAAGGCACTTACACCTTGGCGGTCAACAATACCGGCAACG 3013
 999 nLysSerAla..... 1002

3014 AACCTGCAAGCCTCGAACAATTGACGGTAGTGGAAGGAAAAGACAACAAA 3063
1003 .....ThrGlyHisAspAsn... 1007

3064 CCGCTGTCCGAAAACCTTAATTTCACCCTGCAAAACGAACACGTCGATGC 3113
1008 ......SerIleTrpValAsnPhe..... 1013

3114 CGGCGCGTGGCGTTACCAACTCATCCGCAAAGACGGCGAGTTCCGCCTGC 3163
1013 ..... 1013

3164 ATAATCCGGTCAAAGAACAAGAGCTTTCCGACAAACTCGGCAAGGCAGAA 3213
1013 ..... 1013

3214 GCCAAAAAACAGGCGGAAAAAGACAACGCGCAAAGCCTTGACGCGCTGAT 3263
1014 LeuLysLysProSerAspLysAsp.....ThrLeuAspIleProLe 1027

3264 TGCGGCCGGGCGCGATGCCGTCGAAAAGACAGAAAGCGTTGCCGAACCGG 3313
1027 u.....ValSerAlaProGluAlaThrAlaAspAsnL 1038

3314 CCCGGCAGGCAGGCGGGGAAAATGTCGGCATT..... 3345
1038 euPheArgAlaSerThrArgValValGlyPheSerAspValThrProThr 1054

3346 ......ATGCAGGCGGAGGAAGAGAAAAAACGGGTGCAGGCGGATAAAGA 3389
1055 LeuSerValArgLysGluAspGlyLysLysGluTrpValLeuAsp..... 1069

3390 CACCGCCTTGGCGAAACAGCGCGAAGCGGAAACCCGGCCGGCTACCACCG 3439
1069 ..... 1069

3440 CCTTCCCCCGCGCCCGCCGCGCCCGCCGGGATTTGCCGCAACTGCAACCC 3489
1070 ........GlyTyrGlnValAlaArgAsnAsp..... 1077

3490 CAACCGCAGCCCCAACCGCAGCGCGACCTGATCAGCCGTTATGCCAATAG 3539
1078 ..............GlyGlnGlyLysAlaAlaAlaThrPheMetHisIl 1089

3540 CGGTTTGAGTGAATTTTCCGCCACGCTCAACAGCGTTTTCGCCGTACAGG 3589
1089 eSerTyrAsnAsnPheIleThrGluValAsnAsnLeuAsnLysArgMetG 1106
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3640 ..............AGCGGCATCCGGGAC.....ACCAAACACTA 3665
1120 ArgLeuLeuAsnGlySerGlySerAlaAspGlyGlyPheThrAspHisTy 1136

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1136 r.....ThrLeuLeuGlnM 1141

3716 TCGGTATGCAGAAA......AACCTCGGCAGCGGGCGCGTC......GGC 3753
1141 etGlyAlaAspArgLysHisGluLeuGlySerMetAspLeuPheThrGly 1157

3754 ATCCTGTTTTCGCACAACCGGACCGAAAACACCTTCGACGACGGCATCGG 3803
1158 ValMetAlaThrTyrThrAspThrAsp..... 1166

3804 CAACTCGGCACGGCTTGCCCACGGCGCCGTTTTCGGGCAATACGGCATCG 3853
1167 .AlaSerAlaGlyLeuTyrSerGlyLysThrLysSerTrpGlyGly.... 1181

3854 ACAGGTTCTACATCGGCATCAGCGCGGGCGCGGGTTTTAGCAGCGGCAGC 3903
1182 .....GlyPheTyrAlaSerGlyLeuPheArgSerGlyAla 1193

3904 CTTTCAGACGGCATCGGAGGCAAAATCCGCCGCCGCGTGCTGCATTACGG 3953
1194 TyrPheAspLeuIleAlaLysTyrIleHisAsn..... 1204

3954 CATTCAGGCACGATACCGCGCCGGTTTCGGCGGATTCGGCATCGAACCGC 4003
1205 ....GluAsnLysTyrAspLeuAsnPheAlaGlyAlaGlyLysGlnAsnP 1220

4004 ACATCGGCGCAACGCGCTATTTCGTCCAAAAAGCGGATTACCGCTACGAA 4053
1220 heArgSerHisSerLeuTyrAlaGlyAlaGluValGlyTyrArgTyrHis 1236

4054 ......AACGTCAATATCGCCACCCCC..... 4074
1237 LeuThrAspThrThrPheValGluProGlnAlaGluLeuValTrpGlyAr 1253

4075 .......GGCCTTGCATTCAACCGCTACCGCGCGGGCATTAAGGCAGATT 4117
1253 gLeuGlnGlyGlnThrPheAsnTrpAsnAspSerGlyMet......AspV 1268

4118 ATTCATTCAAACCGGCGCAACACATTTCCATCACGCCTTATTTGAGCCTG 4167
1268 alSerMetArg.....ArgAsnSerValAsnProLeu......Val 1279

4168 TCCTATACCGATGCCGCTTCGGGCAAAGTCCGAACACGCGTCAATACCGC 4217
1280 GlyArgThrGlyValValSerGlyLysThrPheSerGlyLysAspTrpSe 1296

4218 CGTATTGGCTCAG.....GATTTCGGCAAAACCCGCAGTG 4252
1296 rLeuThrAlaArgAlaGlyLeuHisTyrGluPheAspLeuThrAspSerA 1313

4253 CGGAA 4257
1313 laAsp 1314
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seq_documentation_block:

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AC   AAW27705;
XX
DT   08-MAY-1998  (first entry)
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DE   H. influenzae Hap protein autotransporter membrane integration region.
XX
KW   Hap protein; autotransporter; Gram-negative bacteria; diagnostic;
KW   therapy; surface presented polypeptide.
XX
OS   Haemophilus influenzae.
XX
PN   WO9735022-A1.
XX
PD   25-SEP-1997.
XX
PF   15-MAR-1996;   96WO-EP01130.
XX
PR   15-MAR-1996;   96WO-EP01130.
XX
PA   (PLAC ) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN.
XX
PI   Jose J,  Maurer J,  Meyer TF;
XX
DR   WPI; 1997-480227/44.
DR   N-PSDB; AAT88142.
XX
PT   Presentation of peptide(s) on surface of Gram-negative bacteria -
PT   via transformation with vector encoding signal peptide, presented
PT   peptide and transporter domain of auto-transporter, producing
PT   peptide libraries for epitope mapping
XX
PS   Claim 8; Fig 9; 84pp; German.
XX
CC   This sequence represents the H. influenzae Hap autotransporter membrane
CC   integration region. This region is involved in a novel method which
CC   allows the presentation of stable fusion polypeptides on the surface of
CC   Gram-negative bacteria which can be released into the surrounding media.
CC   The method can be used to produce a variegated population of
CC   surface-presented polypeptides, so that bacteria expressing polypeptides
CC   with particular properties can be identified and simultaneously selected,
CC   e.g. for epitope mapping or selection of ligands with the highest
CC   affinity for antibodies, major histocompatibility complex (MHC) molecules
CC   or other components of the immune system. Selected polypeptides can be
CC   used diagnostically, e.g. to screen sera or antibody banks, and
CC   polypeptide expressing cells may be used as live vaccines. They may also
CC   be used therapeutically, e.g. when the polypeptide is an antibody, to
CC   remove or concentrate pollutants, inactivate toxins, prepare and process
CC   food, prepare washing compositions and label cells. Selected bacteria can
CC   be stored, reproduced and replicated on a large scale as individual
CC   clones.
XX
SQ   Sequence   323 AA;
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            Quality:  715.50              Length:    307
              Ratio:  2.909                 Gaps:      1
 Percent Similarity:  80.130   Percent Identity: 43.974

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      33 gLysGlnLysAspLeuIleSerArgTyrSerAsnSerAlaLeuSerGluL 50

    3554 TTTCCGCCACGCTCAACAGCGTTTTCGCCGTACAGGACGAATTAGACCGC 3603
      50 euSerAlaThrValAsnSerMetLeuSerValGlnAspGluLeuAspArg 66
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   67 LeuPheValAspGlnAlaGlnSerAlaValTrpThrAsnIleAlaGlnAs 83

 3654 CACCAAACACTACCGTTCGCAAGATTTCCGCGCCTACCGCCAACAA...A 3700
      |   :::::::|||   |||:::   |||||||||||||:::||||||   |   :
   83 pLysArgArgTyrAspSerAspAlaPheArgAlaTyrGlnGlnGlnLysT 100

 3701 CCGACCTGCGCCAAATCGGTATGCAGAAAAACCTCGGCAGCGGGCGCGTC 3750
      ||:::||||||||||||||||:::||||||   |||::::::||||||:::
  100 hrAsnLeuArgGlnIleGlyValGlnLysAlaLeuAlaAsnGlyArgIle 116

 3751 GGCATCCTGTTTTCGCACAACCGGACCGAAAACACCTTCGACGACGGCAT 3800
      |||   :::|||||||||:::|||::::::|||||||||||||:::   ::
  117 GlyAlaValPheSerHisSerArgSerAspAsnThrPheAspGluGlnVa 133

 3801 CGGCAACTCGGCACGGCTTGCCCACGGCGCCGTTTTCGGGCAATACGGCA 3850
      :   |||   |||   |||:::      :::   |||:::||||||
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           :::   :::|||:::::::::|||:::|||:::|||::::::
  150 rpGlyAspLeuGlnPheGlyValAsnValGlyThrGlyIleSerAlaSer 166

 3901 AGCCTTTCAGACGGCATCGGAGGCAAAATCCGCCGCCGCGTGCTGCATTA 3950
      ::::::::::::      :::   ||||||:::|||:::::::::::||
  167 LysMetAlaGluGluGlnSerArgLysIleHisArgLysAlaIleAsnTy 183

 3951 CGGCATTCAGGCACGATACCGCGCCGGTTTCGGCGGATTCGGCATCGAAC 4000
      ||||::::::|||   |||:::      :::|||   :::||||||:::|
  183 rGlyValAsnAlaSerTyrGlnPheArgLeuGlyGlnLeuGlyIleGlnP 200

 4001 CGCACATCGGCGCAACGCGCTATTTCGTCCAAAAAGCGGATTACCGCTAC 4050
      ||:::::::|||:::::|||||||||:::::::::   :::|||:::
  200 roTyrPheGlyValAsnArgTyrPheIleGluArgGluAsnTyrGlnSer 216

 4051 GAAAACGTCAATATCGCCACCCCCGGCCTTGCATTCAACCGCTACCGCGC 4100
      |||:::|||::::::   ||||||:::|||||||||||||||||:::||
  217 GluGluValArgValLysThrProSerLeuAlaPheAsnArgTyrAsnAl 233

 4101 GGGCATTAAGGCAGATTATTCATTCAAACCGGCGCAACACATTTCCATCA 4150
      |||||||:::::|||||||:::|||   |||:::::::::||||||:::
  233 aGlyIleArgValAspTyrThrPheThrProThrAspAsnIleSerValL 250

 4151 CGCCTTATTTGAGCCTGTCCTATACCGATGCCGCTTCGGGCAAAGTCCGA 4200
        ||||||:::   :::::::|||:::|||:::::::::::::::|||:::
  250 ysProTyrPhePheValAsnTyrValAspValSerAsnAlaAsnValGln 266

 4201 ACACGCGTCAATACCGCCGTATTGGCTCAGGATTTCGGCAAAACCCGCAG 4250
      |||   ||||||   :::|||||||   |||   ||||||:::      ::
  267 ThrThrValAsnLeuThrValLeuGlnGlnProPheGlyArgTyrTrpGl 283

 4251 TGCGGAATGGGGCGTAAACGCCGAAATCAAAGGTTTCACGCTGTCCCTCC 4300
      :   |||   |||:::::|||||||||      |||   :::|||
  283 nLysGluValGlyLeuLysAlaGluIleLeuHisPheGlnIleSerAlaP 300

 4301 ACGCTGCCGCCGCCAAAGGCCCGCAACTGGAAGCGCAACACAGCGCGGGC 4350
         :::   ::::::|||   ||||||      |||:::::::::|||
  300 heIleSerLysSerGlnGlySerGlnLeuGlyLysGlnGlnAsnValGly 316

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  317 ValLysLeuGlyTyrArgTrp 323

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seq_documentation_block:
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XX
AC   AAP80136;
XX
DT   09-OCT-1990  (first entry)
XX
DE   Neisseria IgA-Protease precursor protein.
XX
KW   IgA-Protease precursor; Neisseria sp;
KW   Gram-negative bacterial live vaccines.
XX
OS   Neisseria gonorrhoeae (strain SMH).
XX
FH   Key             Location/Qualifiers
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FT                   /label=IgA-Protease cleavage site (a)
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FT                   /label=IgA-Protease cleavage site (b)
FT   Cleavage-site   327..332
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PN   DE3622221-A.
XX
PD   14-JAN-1988.
XX
PF   02-JUL-1986;   86DE-3622221.
XX
PR   02-JUL-1986;   86DE-3622221.
XX
PA   (PLAC ) MAX PLANCK GES WISSENSCH.
XX
PI   Meyer TF,  Halter R,  Pohlner J;
XX
DR   WPI; 1988-015104/03.
DR   N-PSDB; AAN80154.
XX
PT   Extracellular prodn. of proteins -
PT   by gram-negative host cells contg. a vector contg. one or more
PT   genes coding the desired protein
XX
PS   Disclosure; ; ; German.
XX
CC   Precursor protein consists of three regions i.e. Amino terminal
CC   leader sequence, IgA protease and a "helper" domain. The cleavage
CC   sites given in the features lie in the region between the latter
CC   two domains. DNA encoding a desired protein can be cloned into the
CC   corresponding region in the IgA protease precursor gene, between
CC   the DNA that encodes the natural cleavage sites. Thus, IgA protease
CC   coding region is not disrupted and the desired protein is released
CC   following cleavage by the protease.
XX
SQ   Sequence   741 AA;


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 Percent Similarity:  46.134   Percent Identity: 21.800

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       1 LeuSerAspLysAlaLeuAsnSerPheAspAlaThrProIleAsnGlyAs 17

    2571 TGTCTCCCTAGCCGATAAGGCAGTATTCCATTTTGAAAGCAGCCGCTTTA 2620
         ||||:::|||   ::::::|||::::::   :::   :::::   :::
      17 nValAsnLeuAsnGlnAsnAlaAlaLeuValLeuGlyLysAlaAlaLeuT 34

    2621 CCGGACAAATCAGCGGCGGCAAGGATACGGCATTACACTTA...AAAGAC 2667
           |||:::|||:::|||      ::::::   :::   |||   :::
      34 rpGlyLysIleGlnGlyGlnGlyAsnSerArgValSerLeuAsnGlnHis 50

    2668 AGCGAATGGACGCTGCCGTCAGGCACGGAATTAGGCAATTTAAACCTTGA 2717
         |||:::|||   |||   :::   :::::::::   ||||||:::|||
      51 SerLysTrpHisLeuThrGlyAspSerGlnValHisAsnLeuSerLeuAl 67
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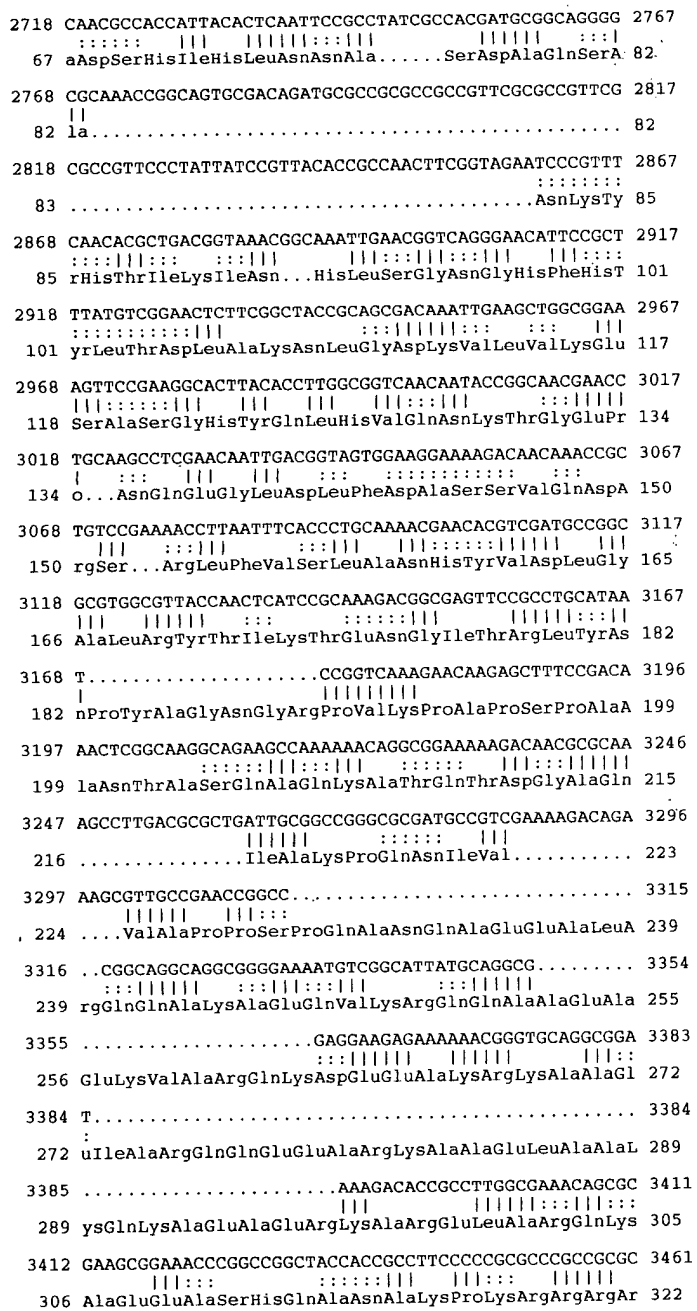
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67 aAspSerHisIleHisLeuAsnAsnAla.....SerAspAlaGlnSerA 82
2768 CGCAAACCGGCAGTGCGACAGATGCGCCGCGCCGCCGTTCGCGCCGTTCG 2817
82 la..... 82
2818 CGCCGTTCCCTATTATCCGTTACACCGCCAACTTCGGTAGAATCCCGTTT 2867
83 .....AsnLysTy 85
2868 CAACACGCTGACGGTAAACGGCAAATTGAACGGTCAGGGAACATTCCGCT 2917
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118 SerAlaSerGlyHisTyrGlnLeuHisValGlnAsnLysThrGlyGluPr 134
3018 TGCAAGCCTCGAACAATTGACGGTAGTGGAAGGAAAAGACAACAAACCGC 3067
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3118 GCGTGGCGTTACCAACTCATCCGCAAAGACGGCGAGTTCCGCCTGCATAA 3167
166 AlaLeuArgTyrThrIleLysThrGluAsnGlyIleThrArgLeuTyrAs 182
3168 T.....CCGGTCAAAGAACAAGAGCTTTCCGACA 3196
182 nProTyrAlaGlyAsnGlyArgProValLysProAlaProSerProAlaA 199
3197 AACTCGGCAAGGCAGAAGCCAAAAAACAGGCGGAAAAAGACAACGCGCAA 3246
199 laAsnThrAlaSerGlnAlaGlnLysAlaThrGlnThrAspGlyAlaGln 215
3247 AGCCTTGACGCGCTGATTGCGGCCGGGCGCGATGCCGTCGAAAAGACAGA 3296
216 .....IleAlaLysProGlnAsnIleVal..... 223
3297 AAGCGTTGCCGAACCGGCC..... 3315
224 ....ValAlaProProSerProGlnAlaAsnGlnAlaGluGluAlaLeuA 239
3316 ..CGGCAGGCAGGCGGGGAAAATGTCGGCATTATGCAGGCG..... 3354
239 rgGlnGlnAlaLysAlaGluGlnValLysArgGlnGlnAlaAlaGluAla 255
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3384 T..... 3384
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3385 .....AAAGACACCGCCTTGGCGAAACAGCGC 3411
289 ysGlnLysAlaGluAlaGluArgLysAlaArgGluLeuAlaArgGlnLys 305
3412 GAAGCGGAAACCCGGCCGGCTACCACCGCCTTCCCCCGCGCCCGCCGCGC 3461
306 AlaGluGluAlaSerHisGlnAlaAsnAlaLysProLysArgArgArgAr 322
3462 CCGCCGGGATTTGCCGCAA..... 3480
322 gArgAlaIleLeuProArgProProAlaProValPheSerLeuAspAspT 339
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3480 3480
422 pAsnThrGluLeuHisGluLysValGluThrAlaGlyLeuGlnProArgA 439
3481 ..CTGCAACCCCAACCGCAGCCCCAACCGCAGCGCGACCTGATCAGCCGT 3528
439 laAlaGlnProArgThrGlnAlaAlaAlaGlnAlaAspAlaValSerThr 455
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3577 .....TTCGCCGTACAGGACGAATTAGACCGCGTATTTG 3610
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506 AspTyrAlaSerAlaGlnTyrArgArgPheSerSerLysArgThrGlnTh 522
3711 CCAAATCGGTATGCAGAAAAACCTCGGCAGCGGG...CGCGTCGGCATCC 3757
522 rGlnIleGlyIleAspArgSerLeuSerGluAsnMetGlnIleGlyGlyV 539
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539 alLeuThrTyrSerAspSerGlnHisThrPheAspGlnAla...GlyGly 554
3808 TCGGCACGGCTTGCCCACGGCGCCGTTTTCGGGCAATACGGCATC...GA 3854
555 LysAsnThrPheValGlnAlaAsnLeuTyrGlyLysTyrTyrLeuAsnAs 571
3855 CAGGTTCTACATCGGCATCAGCGCGGGCGCGGGTTTTAGCAGCGGCAGCC 3904
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605 LeuThrLeuGlyAsnThrLeuLysIleAsnGlnPheGluIleValProSe 621
4005 CATCGGCGCAACGCGCTATTTCGTCCAAAAAGCGGATTACCGCTACGAAA 4054

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  621 rAlaGlyIleArgTyrSerArgLeuSerSerAlaAspTyrLysLeuGlyA 638

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  638 spAspSerValLysValSerSerMetAlaValLysThrLeuThrAlaGly 654

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  670 oLeuLeuSerAlaAlaTyrPhe...AlaAsnTyrGlyLysGlyGlyValA 686

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 4305 TGCCGCCGCCAAAGGCCCGCAACTGGAAGCGCAACACAGCGCGGGCATCA 4354
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  719 ySerIleThrLysGlyLysGlnLeuGluLysGlnLysSerGlyGlnIleL 736

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  736 ysIleGlnIleArgPhe 741
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seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2001.DAT:AAG98842

seq_documentation_block:

ID AAG98842 standard; Protein; 1569 AA.
XX
AC AAG98842;
XX
DT 26-SEP-2001 (first entry)
XX
DE E. coli growth and proliferation related protein sequence SEQ ID NO:312.
XX
KW Escherichia coli; growth; proliferation; microbial; antimicrobial;
KW bacterial infection; microorganism.
XX
OS Escherichia coli.
XX
PN WO200134810-A2.
XX
PD 17-MAY-2001.
XX
PF 09-NOV-2000; 2000WO-US30950.
XX
PR 09-NOV-1999; 99US-0164415.
XX
PA (ELIT-) ELITRA PHARM INC.
XX
PI Forsyth RA, Ohlsen K, Zyskind J;
XX
DR WPI; 2001-335933/35.
DR N-PSDB; AAH84513.
XX
PT Novel nucleic acids that inhibit Escherichia coli proliferation, useful
PT for screening for homologous genes and for designing expression vectors
PT -
XX
PS Claim 19; Page 396-399; 522pp; English.
XX
CC AAH84373 to AAH84499 represent Escherichia coli growth and proliferation
CC related DNA sequences (I). AAH84500 to AAH84670 encode the E. coli
CC growth and proliferation related proteins given in AAG99078 and AAG98830
CC to AAG98999. (I) can be used as potential targets for the generation of
CC new antimicrobial agents, and for identification of compounds which
CC interact with the gene products of (I). In addition the expression of
CC (I) and the purification of the proteins, the purified proteins can be
CC used to generate reagents and screen small molecule libraries or other
CC candidate compound libraries for compounds that can be further developed
CC to yield novel antimicrobial compounds. In addition, nucleic acid probes
CC complementary to (I) that are specific for particular species of
CC microorganisms can be used to identify particular microorganism species
CC in clinical specimens, therefore, providing a rapid and dependable
CC method by which to identify the causative agents of a bacterial
CC infection. Also, antibodies generated against proteins translated from
CC mRNA transcribed from proliferation-required sequences can also be used
CC to screen for specific microorganisms that produce such proteins in a
CC species-specific manner. AAH84371 and AAH84670 represent sequencing
CC primers used in the isolation of E. coli growth and proliferation
CC related sequence, which are used in an example from the present
CC invention.
XX
SQ Sequence 1569 AA;

alignment_scores:

Quality:	364.50	Length:	1634
Ratio:	0.485	Gaps:	81
Percent Similarity:	46.022	Percent Identity:	19.951

alignment_block:
US-09-303-518D-649 x AAG98842 ..

Align seg 1/1 to: AAG98842 from: 1 to: 1569

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  113 sGlyGlyValSerAsnGlySerLeuIleGluSerGlyGlyTyrGlnAspI 130

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  180 ThrIleLysGlyGlyAlaSerArgValGluGlyGlySerAlaAsnGlyIl 196

  771 TTTACCAACAGGAGGCTCA............................... 789
      :|||       |||||||||
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              ::::::   |||||||||         :::       :::
  213 lyThrThrIleAsnLysSerGlySerGlnAspValValGlnGlySerLeu 229

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  230 AlaThrAsnThrThrIleAsnGly............GlyArgGlnTyrVa 242

  882 AGGA........................AAAAGCAATGGCTTCCAGC 904
      :                          |||:::::|||   |||
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1040 AACACAATTCTCTGCCTAATAGA........................... 1062
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1063 ..............TTAAAAACACGAACCGTTCAATTGTTTAATGTTTC 1097
 326 HisAspGlyAlaIleLeuLysThrAsnThr.........AsnGlyThrTh 339

1098 TTTATCCGAGACAGCAAGAGAACCTGTTTAT............CATGCTG 1135
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1136 CA.....................GGTGGT.........GTCAACAGTTAT 1155
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1481 ATAAAGGCAAA............AAACAAGCCTTTAGTGAAATCGGCTTG 1518
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 565 LeuAsnAsnGlyGlyValLeuGluValGlnAspGlyGlyGluAlaLysHi 581

1555 ....AATCAGTTCAACCCCGACAAACTCTATTTCGGCTTTCGCGGCGGAC 1600
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 614 AsnSerGluAlaLysAsnValValLeu.........GluAsnAlaGlySe 627

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2217 AAAA.....................................ACCA 2224
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2225 TTACCGACGAT..................................... 2235
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2701 ..............................GGCAATTTAAACCTT... 2715
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2833 ........................TCCGTTACACCGCCAACTTCGG 2854
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2855 TAGAATCCCGTTTCAACACGCTGACGGTAAACGGCAAATTGAACGGTCAG 2904
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3299 GCGTTGCCGAACCGGCCCGGCAGGCAGGCGGGGAAAATGTCGGCATTATG 3348
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1232 ...IleProAsn..................................... 1234

3349 CAGGCGGAGGAAGAGAAAAAACGGGTGCAGGCGGATAAAGACACCGCCTT 3398

1234 ..................................................... 1234

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1235 ................ProLysProAspProLysProAspProLysPro 1245

3449 GCGCCCGCCGCGCCCGCCGGGATTTGCCGCAACTGCAACCCCAACCGCAG 3498
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1246 AspPro..AsnProLysProAsp...ProThrProAspProThrProThr 1260

3499 CCCCAACCGCAGCGCGACCTGATCAGCCGTTATGCCAATAGCGGTTTGAG 3548
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1261 ProValProGluLysArgIleThrPro......SerThrAlaAlaValLe 1275

3549 TGAATTTTCCGCCACGCTCAACAGCGTTTTC..............GCCG 3583
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1275 uAsnMetAlaAlaThrLeuProLeuValPheAspAlaGluLeuAsnSerI 1292

3584 TACAGGACGAATTAGACCGCGTATTTGCCGAAGACCGCCGCAACGCCGTT 3633
     ::::::::::|||:::  :::  |||:::  :::::::|||  |||
1292 leArgGluArgLeuAsnIleMetLysAlaSerProHisAsnAsnAsnVal 1308

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1309 Trp...GlyAlaThrTyrAsnThrArgAsnAsnValThrThrAspAlaGl 1324

3684 CGCCTACCGCCAACAAACCGACCTGCGCCAAATCGGTATGCAGAAAAACC 3733
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1324 yAlaGlyPheGluGlnThr.........LeuThrGlyMetThrValGlyI 1338

3734 TC.......................GGCAGCGGGCGCGTCGGCATCCTG 3759
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  1371 rValGlySerTyrSerLeuGlyGlyTyrAlaSerTrpGluHisGluSerG 1388

  3833 TTTTC.........GGGCAATACGGCATCGACAGGTTC.........TAC  3864
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  1388 lyPheTyrLeuAspGlyValValLysLeuAsnArgPheLysSerAsnVal 1404

  3865 ATCGGCATCAGCGCGGGCGCGGGTTTTAGCAGCGGCAGCCTT...TCAGA  3911
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  1405 AlaGlyLysMetSerSerGlyGlyAlaAlaAsnGlySerTyrHisSerAs 1421

  3912 CGGCATCGGAGGCAAAATCCGCCGCCGCGTGCTGCATTACGGCATTCAGG  3961
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  1421 nGlyLeuGlyGlyHis.........................IleGluT 1429

  3962 CACGATACCGCGCCGGTTTCGGCGGATTCGGCATCGAACCGCACATCGGC  4011
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  1429 hrGlyMetArgPheThrAspGlyAsnTrpAsnLeuThrProTyrAlaSer 1445

  4012 GCAACGCGCTATTTCGTCCAAAAAGCGGATTACCGCTACGAAAAC..... 4056
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  4057 .......GTCAATATCGCCACCCCCGGCCTTGCATTCAACCGCTACCGC.  4098
             ::::::   |||   ::::::            ||||||
  1462 tLysSerLysSerValAspThrArgSerIle.........TyrArgG 1475

  4099 ..GCGGGCATTAAGGCAGATTATTCATTCAAACCGGCGCAACACATTTCC  4146
          |||         :::|||::::::::::   ::::::   ::::::
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  4147 ATCACGCCTTATTTGAGCCTGTCCTATACCGATGCCGCTTCGGGCAAAGT  4196
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  1492 ValGluProTrpLeuLysAlaAlaValArgLysGluPheValAspAspAs 1508

  4197 CCGAACACGCGTCAATACCGCCGTATTGGCTCAGGATTTC......GGCA  4240
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  4341 CAGCGCGGGCATCAAA.................TTAGGCTACCGCTGG  4371
       ||||||||||::::::                ||||   :::|||
  1551 sSerAlaGlyValGluSerProTrpAsnAlaValAlaGlyValAsnTrp 1567
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seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2000.DAT:AAB01830

seq_documentation_block:
ID   AAB01830 standard; Protein; 1222 AA.
XX
AC   AAB01830;
XX
DT   11-SEP-2000  (first entry)
XX
DE   H. influenzae strain K1 mature full-length HMW1A protein, SEQ ID NO:37.
XX
KW   Mature HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW   non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW   recombinant production; Escherichia coli; antibacterial; vaccine;
KW   human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW   detection; diagnosis.
XX
OS   Haemophilus influenzae strain K1.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 307
FT                   /note= "Encoded by GG"
XX
PN   WO200020609-A2.
XX
PD   13-APR-2000.
XX
PF   07-OCT-1999;    99WO-CA00938.
XX
PR   07-OCT-1998;    98US-0167568.
PR   08-DEC-1998;    98US-0206942.
XX
PA   (CONN-) CONNAUGHT LAB LTD.
XX
PI   Loosmore SM,  Yang Y,  Klein MH;
XX
DR   WPI; 2000-303789/26.
DR   N-PSDB; AAA52180.
XX
PT   Nucleic acid molecule for producing recombinant high molecular weight
PT   proteins of Haemophilus which are used as a vaccine to provide
PT   protection against Haemophilus induced diseases in humans -
XX
PS   Claim 8; Fig 20A-R; 307pp; English.
XX
CC   The invention relates to the recombinant production of Haemophilus
CC   influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC   expression construct used to effect recombinant expression comprises a
CC   promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC   to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC   influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC   clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC   hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC   and the hmwB and hmwC genes encode accessory proteins which are
CC   responsible for post-translational processing and secretion of the HMWA
CC   proteins. The modified hmwABC operon used in the expression construct of
CC   the invention contains an A gene modified such that it encodes only the
CC   mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC   and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC   strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC   vectors are used for the production of recombinant H. influenzae HMW
CC   proteins which can be used as vaccines to mediate a humoral or
CC   cell-mediated immune response to provide protection against diseases in
CC   humans caused by H. influenzae (e.g., otitis media, epiglottitis,
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CC   antigens in immunoassays for detecting antibodies against Haemophilus,
CC   HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC   HMW proteins can be used to isolate and clone hmw genes from other
CC   non-typeable strains of Haemophilus via hybridisation reactions. The
CC   present sequence represents a mature HMWA protein from a non-typeable
CC   strain of H. influenzae.
XX
SQ   Sequence   1222 AA;


alignment_scores:
            Quality:  307.00              Length:   1030
              Ratio:  0.594                 Gaps:     50
 Percent Similarity:  50.194   Percent Identity: 21.262

alignment_block:
 US-09-303-518D-649 x AAB01830   ..

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 675 TTGGCTCGTTGGTGGCAAT..........................ACCT 697
      :       |||:::::::::                      |||:
  62 rIleThrValAsnSerAspIleAsnIleGlyAspSerSerHisLeuThrL 79

 698 TTGCACAAAATGGATCAGGTGGTGGCACAGTCAACTTAGGTAGTGAAAAA 747
      ::   ::::::|||:::|||    |||   |||||||:::
  79 euTrpSerGluGlyGlnGlyArgGlyGlyValAsnVal............ 91

 748 ATTAAACATAGCCCATATGGTTTTTTACCAACAGGAGGCTCATTTGGCGA 797
                                  |||||||:::       :::
  92 ..............................ThrGlyAsnIleThrSerTh 98

 798 CAGTGGCTCACCAATGTTTATCTAT...............GATGCCCAAA 832
      :::::::::   :::    ||||||              |||::::::|
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 833 AGCAAAAGTGGTTAATTAATGGGGTATTGCAAACGGGCAACCCCTATATA 882
      ||              |||   :::|||::::::|||        |||
 115 ys...............AsnIleThrLeuLysSerGlyTyrLeuAsnIle 126

 883 GGAAAAAGCAATGGCTTCCAGCTGGTTCGTAAAGATTGGTTCTATGATGA 932
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 127 ThrThrLysGlnGly..................AspIleAlaPheGluAs 137

 933 A.......................ATCTTTGCTGGAGATACCCATTCAG 958
      :                       |||   |||      |||   :::|
 137 pLysProGlyLeuSerAsnLeuThrIleThrAlaLysGlyThrIleAlaV 154

 959 TATTCTACGAACCACGTCAAAATGGGAAATACTCTTTTAACGACGATAAT 1008
      ||                   |||:::|||   :::|||:::   ||||||
 154 al..................AsnAsnLysLysGlyPheArgPheAspAsn 164

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              |||||||||   |||   ::::::   |||:::    |||
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1044 CAATTCTCTGCCTAATAGATTAAAAACACGAACCGTTCAATTGTTTAATG 1093
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 181 rGlyAsnArgAspSerAsnPheGluThrHisPheArgGlyArgLeuAsnI 198

1094 TTTCT..............TTATCCGAGACAGCAAGAGAACCTGTTTAT 1128
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1129 CATGCTGCAGGTGGTGTCAACAGTTATCGA...CCCAGACTGAATAATGG 1175
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 215 ArgArgHisTrpGlyArgSerHisTrpAsnValThrArgLeuAsnValSe 231

1176 AGAAAATATTTCCTTT.........ATTGACGAA................ 1200
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 231 rGluAsnSerTyrPheAsnValThrIleAspSerSerGlySerAlaSerS 248

1201 .....GGAAAAGGCGAATTGATACTTACCAGCAACATCAATCAAGGTGCT 1245
           |||   |||   |||                 |||    ::::::|||
 248 erProGlyAlaGlyProLeu............AsnAlaGlnSerGlyLeu 260

1246 GGAGGATTATATTTCCAAGGAGAT.......................... 1269
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 261 AsnGlyIleSerPheAsnAsnAspThrValPheAsnIleAlaAlaSerSe 277

1270 ..........TTTACGGTCTCGCCT.....................GAAA 1288

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 277 rAlaValAsnPheAsnIleLysProProIleValAspLysValThrAsnG 294

1289 ATAACGAAACTTGGCAAGGCGCGGGCGTTCATATCAGTGAAGACAGTACC 1338
      :::|||:::|||              :::::::::   :::      :::
 294 lyAsnHisThrLeuPheLysGlyAsnIleSerValLeuGlyGlyGlyAsp 310

1339 GTTACTTGGAAAGTAAACGGC............................. 1359
      |||::::::      |||:::
 311 ValAsnPheHisPheAsnAlaSerSerSerAsnTyrGlnThrTyrGlyVa 327

1360 ....GTGGCAAACGACCGCCTGTCCAAAATCGGCAAAGGCACGCTGCACG 1405
         :::   ::::::::::::|||       |||   ::::::|||
 327 lIleIleGluSerGlnAsnPheSerAlaSerGlyGlySerSerLeuLysP 344

1406 TTCAAGCCAAAGGGGAAAACCAAGGCTCGATCAGCGTGGGCGAC...... 1449
      ::::::::|||:::::::::::::::::::::::::   :::
 344 heLysSerGluGlySerThrHisAlaAlaPheThrIleLysAsnAspLeu 360

1450 ..................GGTACAGTCATTTTGGATCAGCAGGCA..... 1476
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 361 IleLeuAsnAlaThrGlyGlyAsnIleSerLeuAsnGlnValAlaGlyIl 377

1477 .GACGATAAAGGCAAAAAACAAGCCTTTAGTGAAATCGGCTTGGTCAGCG 1525
       |||::::::   ||||||:::   :::::::::   :::::::::
 377 eAspSerAsnLeuLysLysSerLeuIleAlaAsnLysAsnIleThrPheG 394

1526 GCAGGGGTACGGTGCAACTGAATGCCGATAATCAGTTCAACCCCGACAAA 1575
         |||::::::   |||   |||                     ||||||
 394 luGlyGlyAsnIleThrLeuAlaAla.................AspLys 404

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           :::   :::::::|||:::             :::|||   :::::
 405 LysProIleGluIleLysGlyAsnIleThrValLysGluGlyAlaAsnVa 421

1626 TTCGTTCCACCGTATTCAA...AATACCGATGAAGGGGCGATGATTGTCA 1672
      :::::::::      :::   ::::::|||::::::|||:::    ::::
 421 lThrLeuArgSerAlaAsnTyrGlyAsnAspLysSerAlaLeuSerIleA 438

1673 ACCACAATCAAGACAAAGAATCCACCGTTACCATTACAGGCAAT...... 1716
      ::    |||       :::::::::::::::|||:::|||||||:::
 438 rgGlyAsnValThrAsnLysGlyAsnLeuThrValThrGlySerAlaIle 454

1717 .........AAAGATATTGCTACAACCGGCAAT................ 1740
              |||:::::::::::   |||:::
 455 AsnIleGluLysAsnLeuThrValGluGlySerAlaLysPheLeuAlaAs 471

1741 ..................................AACAACAGCTTGGATA 1756
                                      :::|||:::      |
 471 nProAsnTyrSerPheAsnValSerGlyLeuPheAspAsnGlnGlyLysS 488

1757 GCAAAAAAGAAATTGCCTACAACGGTTGGTTTGGCGAGAAAGATACGACC 1806
      ||:::   :::||||||   :::|||   :::       ||||||
 488 erAsnIleSerIleAlaLysGlyGlyAlaIle...PheLysAspIleGlu 503

1807 AAAACGAACGGGCGGCTCAACCTTGTTTACCAGCCCGCCGCAGAAGACCG 1856
      :::|||   |||   |||||||::::::   :::       ::::::   ::
 504 AsnThr...GlySerLeuAsnIleThrThrLysSerAspSerAsnHisHi 519

1857 CACCCTGCTGCTTTCCGGCGGAACAAATTTAAACGGCAACATCACGCAAA 1906
      :|||::::::   ::::::   ||||||   :::|||:::::::::   |
 519 sThrIleIleLysGlyAsnIleThrAsnArgLysGlyAspLeuAsnIleT 536

1907 CAAACGGCAAACTGTTTTTCAGCGGCAGACCAACACCGCACGCCTACAAT 1956
      |||||                 :::|||      |||
 536 hrAsn...............AsnGlyAspAsnThrGlu.........Ile 544

1957 CATTTAAACGACCATTGGTCGCAAAAAGAGGGCATTCCTCGCGGGGAAAT 2006
      :::::::::   :::   ||||||||||||              |||:::::
 545 GlnIleGlyGlyAsnIleSerGlnLysGlu...........GlyAsnLe 557

2007 CGTGTGGGACAACGACTGGATCAACCGCACATTTAAAGCGGAAAACTTCC 2056
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 557 uThrIleSerSerAspLysValAsnIleThr.........GluArgIleT 571

2057 AAATTAAAGGCGGA.......................CAGGCGGTGGTT 2082
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 571 hrIleLysAlaGlyValAsnGlyAspAsnSerAspSerAsnGluAlaThr 587

2083 TCCCGCAATGTTGCC..................AAAGTGAAAGGCGATTG 2114
     |||   |||::::::                  |||:::   :::|||
 588 SerAlaAsnLeuThrIleLysThrLysGluLeuLysLeuThrAsnAspLe 604

2115 GCATTTGAGCAATCACGCCCAAGCAGTTTTTGGTGTCGCACCGCATCAAA 2164
      ::::::|||:::      :::|||   :::   :::      :::::::
 604 uAsnIleSerGlyPheAsnLysAlaGluIleThrAlaLysAspAsnSerA 621

2165 GCCACACAATCTGTACACGTTCGGACTGGACGGGTCTGACAAATTGTGTC 2214
     ::   ||||||      :::|||||||   :::|||   |||::::::
 621 snLeuThrIleGlyAspAsnSerAsp...AlaGlyAsnThrAspAlaLys 636

2215 GAAAAAACC.........ATTACCGACGATAAAGTGATTGCTTCA..... 2250
     :::   |||          :::   |||:::|||:::   ||||||
 637 LysValThrPheSerAsnValLysAspSerLysIleSerAlaSerAspHi 653

2251 .............TTGACTAAGACCGACATCAGCGGCAATGTCGATCTTG 2287
                  :::|||::::::   ||||||:::::|||   :
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2288 CCGATCACGCTCATTTAAATCTCACAGGGCTT.................. 2319
     :::::   :::      |||   |||||||||
 670 hrGluAspGlyGlyAsnAsnAsnThrGlyLeuThrIleThrAlaLysAsn 686

2320 GCCACACTCAACGGCAATCTTAGTGCAAATGGCGATACACGTTATACAGT 2369
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 687 ValThrValAsnAsnAsnIleThrSerHisLysThrValAsnIleThrAl 703

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     ||:::::::::::::|||   :::   :::   :::::::||
 720 lySerValGluValThrAlaLysThrGlyAspIleLysGlyGlyIleGlu 736

2452 ..................AACACATCGGCTTCGGGCAATGCTTCATTTAA 2483
                         |||   :::||||||||||:::   :::::::||
 737 SerAsnSerGlyAsnValAsnIleThrAlaSerGlyAsp...ThrLeuAs 752

2484 TCTAAGCGACCACGCCGTACAAAACGGCAGTCTGACGCTTTCCGGCAACG 2533
     |:::|||:::   :::   ||||||   :::::::::   :::::::::|
 752 nValSerAsnIleThrGlyGlnAsnValThrValAlaAlaAlaSerGlyA 769

2534 CTAAGGCAAACGTAAGCCATTCCGCACTCAAC.........GGTAATGTC 2574
     ||   ::::::::::::   |||:::::::|||         |||||||:::
 769 laValThrThrThrLysGlySerThrIleAsnAlaThrThrGlyAsnAla 785

2575 TCCCTAGCCGATAAGGCAGTATTCCATTTTGAAAGCAGCCGCTTTACCGG 2624
     :::::::::   |||                                |||||
 786 AsnIleThrThrLys.............................ThrGl 792

2625 ACAAATCAGCGGCGGCAAGGATACGGCA.........TTACACTTAAAAG 2665
     |:::|||:::|||         :::|||         :::::::::
 792 yGluIleAsnGlyGluValLysSerAlaSerGlyAsnValAsnIleThrA 809

2666 ACAGCGAATGGACGCTGCCGTCAGGCACGGAATTAGGCAATTTAAACCTT 2715
       |||      ||||||            :::::::::|||::::::
 809 laSerGlyAsnThrLeu............AsnValSerAsnIleThrGly 821

2716 GACAACGCCACCATTACACTCAATTCCGCCTATCGCCACGATGCGGCAGG 2765
     :::|||:::|||:::|||   ||||||:::           :::   ||
 822 GlnAsnValThrValThrAlaAsnSerGlyAlaIleThrThrThrGluGl 838

2766 GGCGCAAACCGGCAGTGCGACA...GATGCGCCGCGCCGCCGTTCGCGCC 2812
     |:::      :::::::::|||   ||||||
 838 ySerThrIleAsnAlaThrThrGlyAspAla..................  848

2813 GTTCGCGCCGTTCCCTATTATCCGTTACACCGCCAACTTCGGTAGAATCC 2862

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2863 CGTTTCAACACGCTGACGGTAAACGGCAAATTGAACGGTCAGGGAACATT 2912
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2913 CCGCTTTATGTCGGAACTCTTCGGCTACCGCAGCGACAAATTGAAGCTGG 2962
                                                      :
 861 ..................................................V 861

2963 CGGAAAGTTCCGAAGGCACTTACACCTTGGCGGTCAACAAT......... 3003
     ::||||||||||:::|||:::   ||||||   :::::::::
 861 alGluSerSerSerGlySerValThrLeuIleAlaThrGlyGlnThrLeu 877

3004 ...ACCGGCAACGAACCTGCAAGCCTCGAACAATTGACGGTAGTGGAAGG 3050
        :::||||||      ::::::         :::|||:::   :::||
-878 AlaValGlyAsnIleSerGlyAspThrValThrIleThrAlaAspLysGl 894

3051 AAAAGACAACAAACCGCTGTCCGAAAACCTTAATTTCACC 3090
     ||||   :::         |||::::::::::|||   |||
 894 yLysLeuThrThrGlnThrSerSerLysIleAsnGlyThr 907
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seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2000.DAT:AAB01828

seq_documentation_block:

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ID   AAB01828 standard; Protein; 1228 AA.
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AC   AAB01828;
XX
DT   11-SEP-2000  (first entry)
XX
DE   Haemophilus influenzae strain K1 full-length HMW1A protein, SEQ ID NO:34.
XX
KW   HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW   non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW   recombinant production; Escherichia coli; antibacterial; vaccine;
KW   human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW   detection; diagnosis.
XX
OS   Haemophilus influenzae strain K1.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 313
FT                   /note= "Encoded by GG"
XX
PN   WO200020609-A2.
XX
PD   13-APR-2000.
XX
PF   07-OCT-1999;   99WO-CA00938.
XX
PR   07-OCT-1998;   98US-0167568.
PR   08-DEC-1998;   98US-0206942.
XX
PA   (CONN-) CONNAUGHT LAB LTD.
XX
PI   Loosmore SM,  Yang Y,  Klein MH;
XX
DR   WPI; 2000-303789/26.
DR   N-PSDB; AAA52179.
XX
PT   Nucleic acid molecule for producing recombinant high molecular weight
PT   proteins of Haemophilus which are used as a vaccine to provide
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XX
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XX
CC   The invention relates to the recombinant production of Haemophilus
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```

```
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CC   clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC   hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC   and the hmwB and hmwC genes encode accessory proteins which are
CC   responsible for post-translational processing and secretion of the HMWA
CC   proteins. The modified hmwABC operon used in the expression construct of
CC   the invention contains an A gene modified such that it encodes only the
CC   mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
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CC   vectors are used for the production of recombinant H. influenzae HMW
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CC   cell-mediated immune response to provide protection against diseases in
CC   humans caused by H. influenzae (e.g., otitis media, epiglottitis,
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CC   antigens in immunoassays for detecting antibodies against Haemophilus,
CC   HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC   HMW proteins can be used to isolate and clone hmw genes from other
CC   non-typeable strains of Haemophilus via hybridisation reactions. The
CC   present sequence represents an HMWA protein from a non-typeable strain of
CC   H. influenzae.
XX
SQ   Sequence   1228 AA;

alignment_scores:
            Quality:  307.00              Length:   1030
              Ratio:  0.594                Gaps:     50
 Percent Similarity:  50.194   Percent Identity: 21.262

alignment_block:
 US-09-303-518D-649 x AAB01828   ..

 Align seg 1/1  to: AAB01828  from: 1  to: 1228

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     615 ATCTGATGAAGATGAGCCCAATAAC.......................... 639
                |||:::   |||||||||
            20 ....ThrGluSerThrProAsnAsnAsnGluTyrAspSerProAsnGlnI 35

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     640 ..............CGCGAAAGTTCATATCATATTGCAAGTGCGTATTC 674
                      |||:::::|||   :::|||:::::::::   ::
      52 GluArgIleLeuLysArgAsnThrSerValAsnIleThrAlaThrLysTh 68

     675 TTGGCTCGTTGGTGGCAAT.........................ACCT 697
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      68 rIleThrValAsnSerAspIleAsnIleGlyAspSerSerHisLeuThrL 85

     698 TTGCACAAAATGGATCAGGTGGTGGCACAGTCAACTTAGGTAGTGAAAAA 747
         ::   ::::::|||:::|||   |||   |||||||:::
      85 euTrpSerGluGlyGlnGlyArgGlyValAsnVal............. 97

     748 ATTAAACATAGCCCATATGGTTTTTTACCAACAGGAGGCTCATTTGGCGA 797
                                 ||||||:::      :::
      98 ............................ThrGlyAsnIleThrSerTh 104

     798 CAGTGGCTCACCAATGTTTATCTAT..............GATGCCCAAA 832
         :::::::::   :::   ||||||              |||:::::::|
     104 rThrAsnGlyAsnLeuThrIleTyrSerGlyGlyTrpValAspValHisL 121

     833 AGCAAAAGTGGTTAATTAATGGGGTATTGCAAACGGGCAACCCCTATATA 882
         ||              |||   :::|||:::::::|||         |||
     121 ys..............AsnIleThrLeuLysSerGlyTyrLeuAsnIle 132

     883 GGAAAAAGCAATGGCTTCCAGCTGGTTCGTAAAGATTGGTTCTATGATGA 932
               ::::::|||                  |||       ::::::::
     133 ThrThrLysGlnGly.................AspIleAlaPheGluAs 143

     933 A.......................ATCTTTGCTGGAGATACCCATTCAG 958
         :                       |||   |||      |||   :::|
     143 pLysProGlyLeuSerAsnLeuThrIleThrAlaLysGlyThrIleAlaV 160

     959 TATTCTACGAACCACGTCAAAATGGGAAATACTCTTTTAACGACGATAAT 1008
         ||                  |||:::|||   :::|||:::   ||||||
     160 al.................AsnAsnLysLysGlyPheArgPheAspAsn 170

    1009 .........AATGGCACA...GGAAAAATCAATGCCAAACAT...GAACA 1043
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     171 ValThrLeuAsnGlyThrGlyGlyGlyLeuSerPheLysTyrIleGluTh 187

    1044 CAATTCTCTGCCTAATAGATTAAAAACACGAACCGTTCAATTGTTTAATG 1093
          ::::::      ::::::::::::|||:::                :::|||:
     187 rGlyAsnArgAspSerAsnPheGluThrHisPheArgGlyArgLeuAsnI 204

    1094 TTTCT..............TTATCCGAGACAGCAAGAGAACCTGTTTAT 1128
         ::|||              |||   ::::::   :::|||
     204 leSerGlyLysValAspIleLeuMetGlnAlaArgGlnGluAsnTrpAsn 220

    1129 CATGCTGCAGGTGGTGTCAACAGTTATCGA...CCCAGACTGAATAATGG 1175
         :::        |||   :::   ::::::      |||||||||   ::
     221 ArgArgHisTrpGlyArgSerHisTrpAsnValThrArgLeuAsnValSe 237

    1176 AGAAAATATTTCCTTT.........ATTGACGAA.............. 1200
         :||||||      |||         ||||||:::
     237 rGluAsnSerTyrPheAsnValThrIleAspSerSerGlySerAlaSerS 254

    1201 .....GGAAAAGGCGAATTGATACTTACCAGCAACATCAATCAAGGTGCT 1245
              |||   |||   |||            |||   :::::::|||
     254 erProGlyAlaGlyProLeu............AsnAlaGlnSerGlyLeu 266

    1246 GGAGGATTATATTTCCAAGGAGAT........................... 1269
         :::|||:::   |||::::::|||
     267 AsnGlyIleSerPheAsnAsnAspThrValPheAsnIleAlaAlaSerSe 283

    1270 ..........TTTACGGTCTCGCCT.....................GAAA 1288
                   |||::::::::::|||                     ::::
     283 rAlaValAsnPheAsnIleLysProProIleValAspLysValThrAsnG 300

    1289 ATAACGAAACTTGGCAAGGCGCGGGCGTTCATATCAGTGAAGACAGTACC 1338
         ::|||:::|||          :::::::::   :::          :::
     300 lyAsnHisThrLeuPheLysGlyAsnIleSerValLeuGlyGlyGlyAsp 316

    1339 GTTACTTGGAAAGTAAACGGC........................... 1359
         |||::::::      |||:::
     317 ValAsnPheHisPheAsnAlaSerSerSerAsnTyrGlnThrTyrGlyVa 333

    1360 ....GTGGCAAACGACCGCCTGTCCAAAATCGGCAAAGGCACGCTGCACG 1405
             :::   ::::::::::::|||      |||   ::::::|||
     333 lIleIleGluSerGlnAsnPheSerAlaSerGlyGlySerSerLeuLysP 350

    1406 TTCAAGCCAAAGGGGAAAACCAAGGCTCGATCAGCGTGGGCGAC...... 1449
           :::::::::|||:::::::::::::::::::::::::::   :::
     350 heLysSerGluGlySerThrHisAlaAlaPheThrIleLysAsnAspLeu 366

    1450 .................GGTACAGTCATTTTGGATCAGCAGGCA..... 1476
                        |||::::::   |||:::|||   |||
     367 IleLeuAsnAlaThrGlyGlyAsnIleSerLeuAsnGlnValAlaGlyIl 383

    1477 .GACGATAAAGGCAAAAAACAAGCCTTTAGTGAAATCGGCTTGGTCAGCG 1525
          |||::::::   |||||||:::   :::::::::   :::::::::
     383 eAspSerAsnLeuLysLysSerLeuIleAlaAsnLysAsnIleThrPheG 400

    1526 GCAGGGGTACGGTGCAACTGAATGCCGATAATCAGTTCAACCCCGACAAA 1575
               |||::::::   |||   |||                |||||||
     400 luGlyGlyAsnIleThrLeuAlaAla.................AspLys 410

    1576 CTCTATTTCGGCTTTCGCGGCGGACGTTTGGATTTAAACGGGCATTCGCT 1625
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          :::   :::::::|||:::             :::|||   :::::
411 LysProIleGluIleLysGlyAsnIleThrValLysGluGlyAlaAsnVa 427

1626 TTCGTTCCACCGTATTCAA...AATACCGATGAAGGGGCGATGATTGTCA 1672
     ::::::::::      :::   :::::::|||:::::|||:::   ::::
 427 lThrLeuArgSerAlaAsnTyrGlyAsnAspLysSerAlaLeuSerIleA 444

1673 ACCACAATCAAGACAAAGAATCCACCGTTACCATTACAGGCAAT...... 1716
     ::   |||       ::::::::::::::|||:::||||||:::   .
 444 rgGlyAsnValThrAsnLysGlyAsnLeuThrValThrGlySerAlaIle 460

1717 .........AAAGATATTGCTACAACCGGCAAT................. 1740
             |||:::::::::::::   |||:::
 461 AsnIleGluLysAsnLeuThrValGluGlySerAlaLysPheLeuAlàAs 477

1741 ................................AACAACAGCTTGGATA 1756
                                    :::|||:::      |
 477 nProAsnTyrSerPheAsnValSerGlyLeuPheAspAsnGlnGlyLysS 494

1757 GCAAAAAAGAAATTGCCTACAACGGTTGGTTTGGCGAGAAAGATACGACC 1806
     ||:::   :::|||||||   :::|||   :::       ||||||
 494 erAsnIleSerIleAlaLysGlyGlyAlaIle...PheLysAspIleGlu 509

1807 AAAACGAACGGGCGGCTCAACCTTGTTTACCAGCCCGCCGCAGAAGACCG 1856
     :::|||   |||   ||||||::::::   :::       ::::::   ::
 510 AsnThr...GlySerLeuAsnIleThrThrLysSerAspSerAsnHisHi 525

1857 CACCCTGCTGCTTTCCGGCGGAACAAATTTAAACGGCAACATCACGCAAA 1906
     :|||::::::   ::::::   ||||||   :::|||:::::::::   |
 525 sThrIleIleLysGlyAsnIleThrAsnArgLysGlyAspLeuAsnIleT 542

1907 CAAACGGCAAACTGTTTTTCAGCGGCAGACCAACACCGCACGCCTACAAT 1956
     |||||                :::|||      |||
 542 hrAsn..............AsnGlyAspAsnThrGlu.........Ile 550

1957 CATTTAAACGACCATTGGTCGCAAAAAGAGGGCATTCCTCGCGGGGAAAT 2006
     :::::::::   :::   ||||||||||||              |||:::::
 551 GlnIleGlyGlyAsnIleSerGlnLysGlu............GlyAsnLe 563

2007 CGTGTGGGACAACGACTGGATCAACCGCACATTTAAAGCGGAAAACTTCC 2056
     ::::   :::::::|||   :::|||   |||         |||::::::
 563 uThrIleSerSerAspLysValAsnIleThr.........GluArgIleT 577

2057 AAATTAAAGGCGGA.......................CAGGCGGTGGTT 2082
       ||||||:::|||                      :::   ::::::
 577 hrIleLysAlaGlyValAsnGlyAspAsnSerAspSerAsnGluAlaThr 593

2083 TCCCGCAATGTTGCC..................AAAGTGAAAGGCGATTG 2114
     |||   |||::::::                  |||:::   :::|||
 594 SerAlaAsnLeuThrIleLysThrLysGluLeuLysLeuThrAsnAspLe 610

2115 GCATTTGAGCAATCACGCCCAAGCAGTTTTTGGTGTCGCACCGCATCAAA 2164
       ::::::|||:::      :::|||   :::   :::       :::::::
 610 uAsnIleSerGlyPheAsnLysAlaGluIleThrAlaLysAspAsnSerA 627

2165 GCCACACAATCTGTACACGTTCGGACTGGACGGGTCTGACAAATTGTGTC 2214
     ::   ||||||      :::|||||||   :::|||   |||:::::::
 627 snLeuThrIleGlyAspAsnSerAsp...AlaGlyAsnThrAspAlaLys 642

2215 GAAAAAACC.........ATTACCGACGATAAAGTGATTGCTTCA..... 2250
     :::   |||          :::   |||:::|||:::   ||||||
 643 LysValThrPheSerAsnValLysAspSerLysIleSerAlaSerAspHi 659

2251 .............TTGACTAAGACCGACATCAGCGGCAATGTCGATCTTG 2287
                  :::|||::::::   ||||||::::::|||   :
 659 sAsnValThrLeuAsnSerLysValGluThrSerGlyAspThrAspSerT 676

2288 CCGATCACGCTCATTTAAATCTCACAGGGCTT.................. 2319
     :::::   :::       |||   |||||||||
 676 hrGluAspGlyGlyAsnAsnAsnThrGlyLeuThrIleThrAlaLysAsn 692

2320 GCCACACTCAACGGCAATCTTAGTGCAAATGGCGATACACGTTATACAGT 2369
     :::|||:::|||:::|||:::::::::::::      ::::::   |||::
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 693 ValThrValAsnAsnAsnIleThrSerHisLysThrValAsnIleThrAl 709

2370 CAGCCACAACGCCACCCAAAACGGCAACCTTAGCCTC.........GTGG 2410
     :|||:::|||:::|||   :::::::::  ::::::         :::|
 709 aSerGluAsnValThrThrLysAlaGlyThrThrIleAsnAlaThrThrG 726

2411 GCAATGCCCAAGCAACATTTAATCAAGCCACATTAAACGGC......... 2451
     ||:::::::::::::|||   :::   :::   :::::::|||
 726 lySerValGluValThrAlaLysThrGlyAspIleLysGlyGlyIleGlu 742

2452 ..................AACACATCGGCTTCGGGCAATGCTTCATTTAA 2483
                       |||   :::||||||||||:::   :::::::||
 743 SerAsnSerGlyAsnValAsnIleThrAlaSerGlyAsp...ThrLeuAs 758

2484 TCTAAGCGACCACGCCGTACAAAACGGCAGTCTGACGCTTTCCGGCAACG 2533
     |:::|||:::   :::   ||||||   :::::::::   :::::::::|
 758 nValSerAsnIleThrGlyGlnAsnValThrValAlaAlaAlaSerGlyA 775

2534 CTAAGGCAAACGTAAGCCATTCCGCACTCAAC.........GGTAATGTC 2574
     ||   :::::::::::::   |||::::::|||         |||||||:::
 775 laValThrThrThrLysGlySerThrIleAsnAlaThrThrGlyAsnAla 791

2575 TCCCTAGCCGATAAGGCAGTATTCCATTTTGAAAGCAGCCGCTTTACCGG 2624
     :::::::::   |||                                  |||||
 792 AsnIleThrThrLys..............................ThrGl 798

2625 ACAAATCAGCGGCGGCAAGGATACGGCA.........TTACACTTAAAAG 2665
     |:::|||:::|||          :::|||          :::::::::
 798 yGluIleAsnGlyGluValLysSerAlaSerGlyAsnValAsnIleThrA 815

2666 ACAGCGAATGGACGCTGCCGTCAGGCACGGAATTAGGCAATTTAAACCTT 2715
       |||      ||||||             :::::::::|||:::::::
 815 laSerGlyAsnThrLeu............AsnValSerAsnIleThrGly 827

2716 GACAACGCCACCATTACACTCAATTCCGCCTATCGCCACGATGCGGCAGG 2765
     :::|||:::|||:::|||   ||||||:::              :::   ||
 828 GlnAsnValThrValThrAlaAsnSerGlyAlaIleThrThrThrGluGl 844

2766 GGCGCAAACCGGCAGTGCGACA...GATGCGCCGCGCCGCCGTTCGCGCC 2812
     |:::   :::::::::|||   ||||||
 844 ySerThrIleAsnAlaThrThrGlyAspAla..................... 854

2813 GTTCGCGCCGTTCCCTATTATCCGTTACACCGCCAACTTCGGTAGAATCC 2862

 854 ..................................................... 854

2863 CGTTTCAACACGCTGACGGTAAACGGCAAATTGAACGGTCAGGGAACATT 2912
           |||      |||   :::|||:::::::||||||:::
 855 ......AsnIleThrThrGlnThrGlyAsnIleAsnGlyLys........ 866

2913 CCGCTTTATGTCGGAACTCTTCGGCTACCGCAGCGACAAATTGAAGCTGG 2962
                                                     :
 867 ..................................................V 867

2963 CGGAAAGTTCCGAAGGCACTTACACCTTGGCGGTCAACAAT......... 3003
     ::||||||||||:::|||:::   ||||||   :::::::::
 867 alGluSerSerSerGlySerValThrLeuIleAlaThrGlyGlnThrLeu 883

3004 ...ACCGGCAACGAACCTGCAAGCCTCGAACAATTGACGGTAGTGGAAGG 3050
        :::|||||||        ::::::         :::|||:::   :::||
 884 AlaValGlyAsnIleSerGlyAspThrValThrIleThrAlaAspLysGl 900

3051 AAAAGACAACAAACCGCTGTCCGAAAACCTTAATTTCACC 3090
     ||||   :::         |||:::::::::|||   |||
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seq_documentation_block:
ID AAY81609 standard; Protein; 1237 AA.
XX
AC AAY81609;
XX

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DT   24-MAY-2000  (first entry)
XX
DE   Streptococcus pneumoniae type 4 protein sequence #109.
XX
KW   Streptococcus pneumoniae; vaccine; screening; protein antigen;
KW   antibacterial; antiinflammatory; meningitis; infection; diagnosis;
KW   pneumococcal disease.
XX
OS   Streptococcus pneumoniae.
XX
PN   WO200006737-A2.
XX
PD   10-FEB-2000.
XX
PF   27-JUL-1999;   99WO-GB02451.
XX
PR   27-JUL-1998;   98GB-0016337.
PR   19-MAR-1999;   99US-0125164.
XX
PA   (MICR-) MICROBIAL TECHNICS LTD.
XX
PI   Gilbert CFG,  Hansbro PM;
XX
DR   WPI; 2000-195300/17.
XX
PT   New Streptococcal protein, useful as a vaccine, for diagnosis of
PT   pneumococcal diseases and for screening agents capable of antagonizing
PT   or inhibiting expression of the protein  -
XX
PS   Claim 1; Page 83; 108pp; English.
XX
CC   AAY81501 to AAY81679 represent specifically claimed protein sequences
CC   isolated from Streptococcus pneumoniae. AAA05407 to AAA05590 represent
CC   specifically claimed nucleotide sequences isolated from S. pneumoniae.
CC   The sequences have antibacterial and antiinflammatory properties.
CC   The protein sequences, and fragments of them, are useful as immunogens
CC   and/or antigens. The nucleotide sequences can be used in vaccines and in
CC   diagnostic assays. The proteins and nucleotides can be useful for the
CC   detection and diagnosis of S. pneumoniae. The protein sequences are also
CC   useful for screening an agent capable of antagonising, inhibiting or
CC   interfering with the function or expression of the proteins in which the
CC   agent is useful for treatment or prophylaxis of S. pneumoniae infection
CC   and meningitis. AAA05591 to AAA05614 represent primers used in the
CC   exemplification of the present invention.
XX
SQ   Sequence   1237 AA;


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              Ratio:  0.514                Gaps:     42
 Percent Similarity:  48.099   Percent Identity: 20.000

alignment_block:
 US-09-303-518D-649 x AAY81609   ..

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    1273 ACGGTCTCGCCTGAAAATAACGAAACTTGGCAAGGCGCGGGCGTTCATAT 1322
          |||   ::   |||:::   :::|||       :::|||::::::   ||
     103 ThrSerAlaSerGluSerAlaSerThr......SerAlaSerThrSerIl 117

    1323 CAGTGAAGACAGTACCGTTACTTGGAAAGTAAACGGCGTGGCAAACGACC 1372
          ||||   :::||||||||||:::   :::   :::::::::|||::::::
     117 eSerAlaSerSerThrValValGlySerGlnThrAlaAlaAlaThrGluA 134

    1373 GCCTGTCCAAAATCGGCAAAGGCACGCTGCACGTTCAAGCCAAAGGGGAA 1422
               :::|||                  |||:::         :::
     134 laThrAlaLys.................LysValGluGluAspArgLys 144

    1423 AACCAAGGCTCGATCAGCGTGGGCGACGGTACAGTCATTTTGGATCAGCA 1472
          :::   :::|||      |||::::::   |||   :::   :::   ||
     145 LysProAlaSerAspTyrValAlaSerValThrAsnVal...AsnLeuGl 160

    1473 GGCAGACGATAAAGGCAAAAAACAAGCC..................... 1500
          |:::      |||   :::|||::::::
     160 nSerTyrAlaLysArgArgLysArgSerValAspSerIleGluGlnLeuL 177

    1501 .........................TTTAGTGAAATCGGCTTGGTCAGC 1524
                                   ||||||          :::|||:::
     177 euAlaSerIleLysAsnAlaAlaValPheSerGlyAsnThrIleValAsn 193

    1525 GGCAGGGGTACGGTGCAACTGAATGCCGATAATCAGTTCAACCCCGACAA 1574
          |||      :::::::::   :::   :::         :::      ||
     194 GlyAlaProAlaIleAsnAlaSerLeuAsnIleAlaLysSerGluThrLy 210

    1575 ACTCTATTTCGGCTTTCGCGGCGGACGTTTGGATTTAAACGGGCATTCGC 1624
          |:::|||              |||      :::|||         :::
     210 sValTyr.........ThrGlyGluGlyValAspSerValTyrArgValP 224

    1625 TTTCGTTCCACCGTATTCAAAATACCGATGAAGGGGCGATGATTGTCAAC 1674
               :::::::::::::::   |||:::::|||:::   ::::::
     224 roIleTyrTyrLysLeuLysValThrAsnAspGlySerLysLeuThr... 239

    1675 CACAATCAAGACAAAGAATCCACCGTTACCATTACA...GGCAATAAAGA 1721
                               |||   |||:::|||      |||
     240 ..................PheThrTyrThrValThrTyrValAsnProLy 250

    1722 TATTGCTACAACCGGCAATAACAACAGCTTGGATAGCAAAAAAGAAATTG 1771
                        ||||||   :::|||:::              :::|||
     250 sThrAsnAspLeuGlyAsnIleSerSerMetArgProGlyTyrSerIleT 267

    1772 CCTACAACGGTTGG..................................... 1785
               :::|||
     267 yrAsnSerGlyThrSerThrGlnThrMetLeuThrLeuGlySerAspLeu 283

    1786 .........TTTGGCGAGAAAGAT...ACGACCAAAACGAACGGGCGGCT 1823
                        |||   |||:::      |||      |||||||||
     284 GlyLysProSerGlyValLysAsnTyrIleThrAspLysAsnGlyArgGl 300

    1824 CAACCTTGTTTACCAGCCCGCCGCAGAAGACCGCACCCTGCTGCTTTCCG 1873
          |||   |||:::   :::            |||:::      :::|
     300 nValLeuSerTyrAsnThrSer............ThrMetThrThrGlnG 313

    1874 GCGGAACAAATTTAAACGGCAACATCACGCAAACAAACGGCAAACTGTTT 1923
          ||:::                |||||   ::::||   ||||||      |||
     313 lySerGlyTyrThrTrpGlyAsnGlyAlaGlnMetAsnGly......Phe 327

    1924 TTCAGCGGCAGACCA.................................... 1938
          |||:::   :::
     328 PheAlaLysLysGlyTyrGlyLeuThrSerSerTrpThrValProIleTh 344

    1939 .........................ACACCGCACGCC.............. 1950
                                   ||||||:::|||
     344 rGlyThrAspThrSerPheThrPheThrProTyrAlaAlaArgThrAspA 361

    1951 ........TACAATCATTTAAACGACCATTGGTCGCAAAAAGAGGGCATT 1992
                 |||::::::|||
     361 rgIleGlyIleAsnTyrPheAsnGly....................... 369

    1993 CCTCGCGGGGAAATCGTGTGGGACAACGACTGGATCAACCGCACATTTAA 2042
               |||::::::|||   ::::::         :::         ::
     370 ...GlyGlyLysValValGluSerSerThrThrSerGlnSerLeuSerGl 385

    2043 AGCGGAAAACTTCCAAATTAAAGGCGGACAGGCGGTGGTTTCCCGCAATG 2092
          ::::::::::::::::::::::::::::::|||::::::   :::
     385 nSerLysSerLeuSerValSerAlaSerGlnSerAlaSerAlaSerAlaS 402

    2093 TTGCCAAAGTGAAAGGCGATTGGCATTTGAGCAATCACGCC......... 2133
          :::::::::::::::::         |||      |||
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    2134 .........................CAAGCAGTTTTTGGTGTCGCACC 2156
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     419 ThrSerAlaSerAlaSerAlaSerThrSerAlaSerValSerAlaSerTh 435
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 1005 roGlnProValArgGlnProGlnGlnValSerGlnArgLeuAsnArgHis 1021

 3756 CCT.....GTTTTCGCACAACCGGACCGAAA 3781
                :::      ||||||:::|||::
 1022 GlnArgValArgProLeuGlnGlnValLeuAlaProGlnProGlnArgGl 1038

 3782 ACACCTTCGACGACGGCATCGGCAACTCGGCACGGCTTGCCCACGGCGCC 3831
      ::::::::::|||   :::||||||                 ::::::|
 1038 nGlnValHisArgLeuGlnArgGlnArgValArgLeuAsnArgHisGlnA 1055

 3832 GTTTTCGGGCAATACGG.....CATCGACAGGTT 3860
      ||   |||   ::::::          :::|||||
 1055 rgValArgProLeuGlnGlnValLeuAlaProGlnProGlnArgGlnGln 1071

 3861 CTACATCGG......CATCAGCGCGGGCGCGGGTTTTAGCAG..... 3896
      :::|||||||      |||||||||   |||   :::   |||
 1072 ValHisArgLeuGlnHisGlnArgValArgProLeuGlnGlnValLeuAl 1088

 3897 .CGGCAGCCTTTCAGACGG......CATCGGAGGCAAAATCCGCCGCCGC 3939
          ||||||   |||:::      ||||||  |||          |
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 3940 GTGCTGCATTACGGCATTCAGGCACGATACCGCGCCGGTTTCGGCGGATT 3989
      ||      :::|||  |||                :::   :::|||:::
 1101 rgGlnArgValArgLeuSer.....GlnHisGlnArgVal 1112

 3990 CGGCAT...CGAACCGCACATCGGCGCAACGCGCTATTTCGTCCAAAAAG 4036
      |||:::   :::   |||||||::          |||   :::
 1113 ArgGlnProGlnGlnAlaHisGlnLeuLeuAsnLeuHisGln..... 1126

 4037 CGGATTACCGCTACGAAAACGTCAATATCGCCACCCCCGGCCTTGCATTC 4086
             |||:::|||:::   |||:::|||:::      |||   :::|
 1127 .....ProValArgGlnProGlnHisArgGln...AlaProGlnLeuG 1140

 4087 AACCGCTACCGCGCGGGCATTAAGGCAGATTATTCATTCAAACCGGCGCA 4136
      ||   :::|||
 1140 lnGlnValPro..... 1143

 4137 ACACATTTCCATCACGCCTTATTTGAGCCTGTCCTATACCGATGCCGCTT 4186

 1143 ..... 1143

 4187 CGGGCAAAGTCCGAACACGCGTCAATACCGCCGTATTGGCTCA...GGAT 4233
          :::::::|||:::   ||||||  ||||||:::   :::
 1144 .ValArgGlnProGlnArgArgGlnValArgArgLeuGlnGlnValProV 1160

 4234 TTCGGCAAAACCCGCAGTGCGGAATGGGGCGTAAACGCCGAAATCAAAGG 4283
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 1160 alArgGlnProGlnGlnValProValArgGlnProGlnArgArgGlnVal 1176

 4284 TTTCACGCTGTCCCTCCACGCTGCCGCCGCCAAAGGCCCGCAACTGGAAG 4333
         :::      |||   :::   :::|||::::::|||:::
 1177 ArgArgProGlnProValHisLeuAsnArgHisGlnProValArgGlnPr 1193

 4334 CGCAACACAGCGCGGGCATCAAATTAGG 4361
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 1193 oGlnGlnValLeuValHisGlnLeuGln 1202

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seq_documentation_block:
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AC   AAR26503;
XX
DT   12-MAR-1993  (first entry)
XX
DE   prn proteins.
XX
KW   B. bronchiseptica; P.68; outer membrane protein; piglet; probe;
KW   atrophic rhinitis; alternative cleavage.
XX
OS   Bordetalla bronchiseptica.
XX
FH   Key             Location/Qualifiers
FT   Protein         35..632
FT                   /label= P.68
FT   Region          266..279
FT                   /label= Repeat_region
FT   Region          570..589
FT                   /label= Repeat_region
FT   Peptide         260..262
FT                   /label= RGD_tripeptide
FT   Peptide         701..703
FT                   /label= RGD_tripeptide
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PN   WO9217587-A.
XX
PD   15-OCT-1992.
XX
PF   27-MAR-1992;   92WO-GB00561.
XX
PR   27-MAR-1991;   91GB-0006568.
XX
PA   (WELL ) WELLCOME FOUND LTD.
XX
PI   Charles IG;
XX
DR   WPI; 1992-366258/44.
DR   N-PSDB; AAQ34566.
XX
PT   DNA encoding a Bordetella bronchiseptica protein - used for
PT   obtaining vaccines for preventing respiratory diseases, partic.
PT   atrophic rhinitis in pigs
XX
PS   Claim 1; Fig 1; 28pp; English.
XX
CC   The sequence given is the P.94 antigen from B. bronchiseptica.  The
CC   P.68 antigen is formed by alternative cleavage of this protein.
CC   P.68 is an outer membrane protein with a molecular weight of 68 kD
CC   which is associated with protection of piglets against atrophic
CC   rhinitis.  The DNA sequence encoding these proteins was derived by
CC   standard recombinant DNA techniques using P.68 probes to isolate the
CC   entire P.94 sequence.
XX
SQ   Sequence   911 AA;


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          Quality:  297.50          Length:   1079
            Ratio:  0.613             Gaps:     50
Percent Similarity:  44.949   Percent Identity: 21.965

alignment_block:
US-09-303-518D-649 x AAR26503   ..

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 1417 GGGGAAAACCAAGGCTCGATCAGCGTGGGCGACGGTACAGTCATTTTGGA 1466
      |||||||:::|||   :::|||   :::
   45 GlyGluArgGlnHisGlyIleHisIle..... 53

 1467 TCAGCAGGCAGACGATAAAGGCAAAAAACAAGCCTTTAGTGAAATCGGCT 1516
       :::|||:::|||      |||   :::   |||   :::
   54 .LysGlnSerAspGlyAlaGlyValArgThrAlaThrGlyThrThrIleL 70

 1517 TGGTCAGCGGCAGGGGTACGGTGCAACTGAATGCCGATAATCAGTTCAAC 1566
        ||||||||||||   :::      :::      :::|||
   70 ysValSerGlyArgGlnAlaGlnGlyValLeuLeuGluAsn..... 83

 1567 CCCGACAAACTCTATTTCGGCTTTCGCGGCGGACGTTTGGATTTAAACGG 1616
                :::   |||:::::::|||   :::      :::||
   84 ...ProAlaAlaGluLeuArgPheGlnAsnGlySerValThrSerSerGl 99

 1617 GCATTCGCTTTCGTTCCACCGTATTCAAAATACCGATGAAGGGGCGATGA 1666
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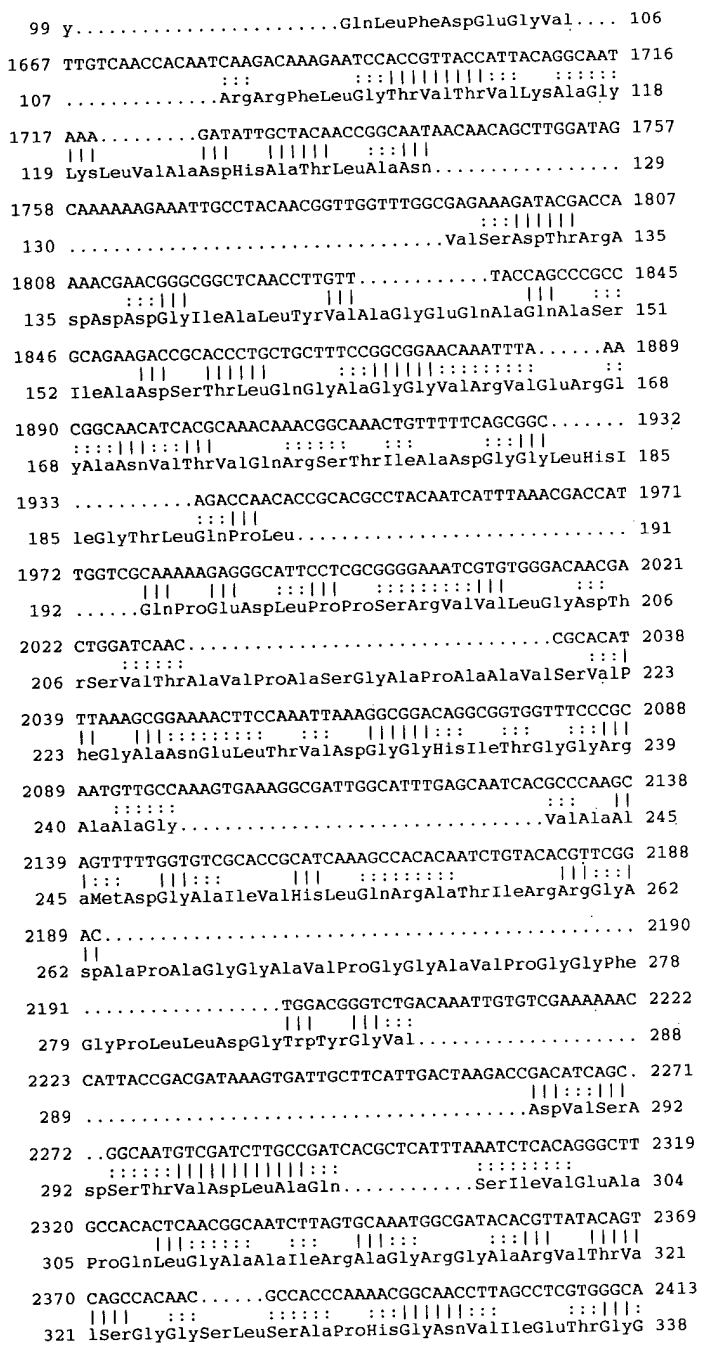

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 559 lyAla.LysAlaProProAlaPro.....................LysPr 568

3316 CGGCAGGCAGGCGGGGAAAATGTCGGCATTATGCAGGCGGAGGAAGAGAA 3365
     |:::   |||   |||
 568 oAlaProGlnProGlyPro.............................. 574

3366 AAAACGGGTGCAGGCGGATAAAGACACCGCCTTGGCGAAACAGCGCGAAG 3415

 574 ..................................................  574

3416 CGGAAACCCGGCCGGCTACCACCGCCTTCCCCCGCGCCCGCCGCGCCCGC 3465
        :::||||||      ||||||    ||||||:::|||||||:::||||
 575 ...GlnProGlyProGlnProProGln.ProProGlnProProGlnProP 590

3466 CGGGATTTGCCGCAACTGCAACCCCAACCGCAGCCCCAACCGCAGCGCGA 3515
     ||                 ||| |||   |||||||||         |||::
 590 roGlnArgGlnProGluAla.ProAlaProGlnProProAlaGlyArgGl 606

3516 CCTGATCAGCCGTTATGCCAATAGCGGTTTGAGTGAATTTTCCGCCACGC 3565
     :|||   |||      ||||||:::::::::::::      ::::::   |
 606 uLeu...SerAlaAlaAlaAsnAlaAlaValAsnThrGlyGlyValGlyL 622

3566 TCAACAGCGTT......TTCGCCGTACAGGACGAATTAGACCGCGTATTT 3609
     ||   |||:::      :::|||   ::::::   |||:::::::   :::
 622 euAlaSerThrLeuTrpTyrAlaGluSerAsnAlaLeuSerLysArgLeu 638

3610 GCCGAAGACCGCCGCAAC............GCCGTTTGGACAAGCGGCAT 3647
     :::|||   |||   |||                :::::::|||      |||::
 639 GlyGluLeuArgLeuAsnProAspAlaGlyGlyAlaTrpGlyArgGlyPh 655

3648 CCGGGACACCAAACACTACCGTTCGCAAGATTTCCGCGCCTACCGCCAAC 3697
     :   :::   ::::::      ::::::      |||   :::   |||:
 655 eAlaGlnArgGlnGlnLeuAspAsnArgAlaGlyArgArgPheAspGlnL 672

3698 AAACCGACCTGCGCCAAATCGGTATGCAGAAAAACCTC............. 3735
     :::::          ::::::|||   :::      :::
 672 ysValAlaGlyPheGluLeuGlyAlaAspHisAlaValAlaValAlaGly 688

3736 GGCAGCGGGCGCGTCGGCATCCTGTTTTCGCACAACCGGACCGAAAACAC 3785
     |||      ::::::|||   |||   :::::::::|||   ::::::
 689 GlyArgTrpHisLeuGlyGlyLeuAlaGlyTyrThrArgGlyAspArgGl 705

3786 CTTC...GACGACGGCATCGGCAACTCGGCACGGCTTGCCCACGGCGCCG 3832
      |||      ||||||   |||:::::   ::::::      |||:::
 705 yPheThrGlyAspGlyGlyGlyHisThrAspAsnValAsnValGlyGlyT 722

3833 TTTTCGGGCAATACGGCATCGACAGGTTCTACATCGGCATCAGCGCGGGC 3882
                ::::   :::   ||||||:::      :::
 722 yrProThrTyrIleAlaAsnSerGlyPheTyrLeuAspAlaThrLeuArg 738

3883 GCGGGTTTTAGCAGCGGCAGCCTT............TCAGACGGC..... 3915
     |||:::      ::::::::::            |||||||||
 739 AlaSerArgLeuGluAsnAspPheLysValAlaGlySerAspGlyTyrAl 755

3916 .ATCGGAGGCAAAATCCGCCGCCGCGTGCTGCATTACGGCATTCAGGCAC 3964
      :::   ||||||   |||               :::|||:::   |||
 755 aValLysGlyLysTyrArgThr............HisGlyValGlyAlaS 768

3965 GATACCGCGCCGGT..............TTCGGCGGATTCGGCATCGAA 3999
        :::||||||                  |||:::   :::|||
 768 erLeuGluAlaGlyArgArgPheAlaHisAlaAspGlyTrpPheLeuGlu 784

4000 CCGCACATCGGCGCAACGCGCTATTTCGTCCAAAAAGCGGATTACCGCTA 4049
     |||:::         :::   :::   |||   ::::::::::||||||
 785 ProGlnAlaGluLeuAlaValPheArgValGlyArgGlySerTyrArgAl 801

4050 CGAAAAC...GTCAATATCGCCACCCCCGGCCTTGCATTCAACCGCTACC 4096
        |||   :::::::::         |||   :::              |
 801 aAlaAsnGlyLeuArgValArgAspGluGlyGlySerSerValLeuGlyA 818

4097 GCGCGGGCATTAAGGCAGATTATTCATTCAAACCGGCGCAACACATTTCC 4146
```

```
        ||   |||::::::::::         ::::::   |||         :::
 818 rgLeuGlyLeuGluValGlyLysArgIleGluLeuAlaGlyGlyArgGln 834

4147 ATCACGCCTTATTTGAGCCTGTCCTATACCGATGCCGCTTCGGGCAAAGT 4196
        :::   ||||||::::::   |||       :::       :::|||
 835 ValGlnProTyrIleLysAlaSerValLeuGlnGluPheAspGlyAlaGl 851

4197 CCGAACACGCGTCAATACCGCCGTATTGGCTCAGGATTTCGGCAAAACCC 4246
        :::|||:::|||       :::       ::::::      ||||
 851 yThrValArgThrAsnGlyIleAlaHisArgThrGluLeuArgGlyThrA 868

4247 GCAGTGCGGAATGGGGCGTAAACGCCGAAATCAAAGGTTTCACGCTGTCC 4296
     ||   ||||||   |||                                |||:::
 868 rg...AlaGluLeuGly.........................LeuGly 874

4297 CTCCACGCTGCCGCCGCCAAAGGCCCGCAACTGGAAGCG......CAACA 4340
     :::   ||||||   :::::::|||   :::|||   |||      :::::
 875 MetAlaAlaAlaLeuGlyArgGlyHisSerLeuTyrAlaSerTyrGluTy 891

4341 CAGCGCGGGCATCAAATTAGGCTACCGCTGG 4371
     :|||   |||   ||||||:::      |||
 891 rSerLysGlyProLysLeuAlaMetProTrp 901
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seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1991.DAT:AAR14320

seq_documentation_block:

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ID   AAR14320 standard; Protein; 911 AA.
XX
AC   AAR14320;
XX
DT   20-JAN-1992  (first entry)
XX
DE   Pertactin antigen P.68.
XX
KW   Pertactin; Pichia; B. pertussis; B. parapertussis.
XX
OS   Bordetella bronchiseptica.
XX
FH   Key             Location/Qualifiers
FT   Peptide         266..270
FT                   /label= repeat
FT   Peptide         271..275
FT                   /label= repeat
FT   Peptide         570..572
FT                   /label= repeat
FT   Peptide         574..576
FT                   /label= repeat
FT   Peptide         578..580
FT                   /label= repeat
FT   Peptide         581..583
FT                   /label= repeat
FT   Peptide         584..586
FT                   /label= repeat
FT   Peptide         587..589
FT                   /label= repeat
FT   Peptide         599..601
FT                   /label= repeat
XX
PN   WO9115571-A.
XX
PD   17-OCT-1991.
XX
PF   28-MAR-1991;   91WO-GB00487.
XX
PR   02-APR-1990;   90GB-0007416.
XX
PA   (WELL ) WELLCOME FOUNDATION LTD.
XX
PI   Clare JJ,  Romanos MA;
XX
DR   WPI; 1991-325214/44.
DR   N-PSDB; AAQ14319.
XX
```

PT Pichia microorganism transformants - for production of
PT Bordetella pertactin antigens for whooping cough vaccines
XX
PS Disclosure; Fig 1B; 38pp; English.
XX
CC Pichia microorganisms are transformed for the expression of
CC pertactin antigens. DNA sequence used are represented in AAQ14319-20
CC encoding the B. bronchiseptica P.68 and B. parapertussis P.70 antigen
CC respectively or the B. pertussis P.69 encoding sequence described
CC by I.G. Charles et al. Proc. Natl. Acad. Sci. USA, Vol. 80:3554-3448
CC (1989).
XX
SQ Sequence 911 AA;

alignment_scores:
Quality: 295.50 Length: 1079
Ratio: 0.612 Gaps: 50
Percent Similarity: 44.764 Percent Identity: 21.965

alignment_block:
US-09-303-518D-649 x AAR14320 ..

Align seg 1/1 to: AAR14320 from: 1 to: 911

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1417 GGGGAAAACCAAGGCTCGATCAGCGTGGGCGACGGTACAGTCATTTTGGA 1466
     ||||||:::|||   :::|||   :::
  45 GlyGluArgGlnHisGlyIleHisIle..................... 53

1467 TCAGCAGGCAGACGATAAAGGCAAAAAACAAGCCTTTAGTGAAATCGGCT 1516
      :::|||:::|||      |||   :::   |||   :::
  54 .LysGlnSerAspGlyAlaGlyValArgThrAlaThrGlyThrThrIleL 70

1517 TGGTCAGCGGCAGGGGTACGGTGCAACTGAATGCCGATAATCAGTTCAAC 1566
      ||||||||||||   :::      :::      :::|||
  70 ysValSerGlyArgGlnAlaGlnGlyValLeuLeuGluAsn......... 83

1567 CCCGACAAACTCTATTTCGGCTTTCGCGGCGGACGTTTGGATTTAAAQGG 1616
                  :::   |||:::::::|||   :::      :::||
  84 ...ProAlaAlaGluLeuArgPheGlnAsnGlySerValThrSerSerGl 99

1617 GCATTCGCTTTCGTTCCACCGTATTCAAAATACCGATGAAGGGGCGATGA 1666
     |                    |||      |||||||||:::
  99 y.....................GlnLeuPheAspGluGlyVal.... 106

1667 TTGTCAACCACAATCAAGACAAAGAATCCACCGTTACCATTACAGGCAAT 1716
                  :::        :::||||||||||:::   :::::
 107 .............ArgArgPheLeuGlyThrValThrValLysAlaGly 118

1717 AAA.........GATATTGCTACAACCGGCAATAACAACAGCTTGGATAG 1757
     |||         |||   ||||||   :::|||
 119 LysLeuValAlaAspHisAlaThrLeuAlaAsn.............. 129

1758 CAAAAAAGAAATTGCCTACAACGGTTGGTTTGGCGAGAAAGATACGACCA 1807
                                          :::|||||||
 130 ..............................ValSerAspThrArgA 135

1808 AAACGAACGGGCGGCTCAACCTTGTT...........TACCAGCCCGCC 1845
       :::|||             |||               |||   :::
 135 spAspAspGlyIleAlaLeuTyrValAlaGlyGluGlnAlaGlnAlaSer 151

1846 GCAGAAGACCGCACCCTGCTGCTTTCCGGCGGAACAAATTTA......AA 1889
        |||   ||||||      :::||||||:::::::::      ::
 152 IleAlaAspSerThrLeuGlnGlyAlaGlyGlyValArgValGluArgGl 168

1890 CGGCAACATCACGCAAACAAACGGCAAACTGTTTTTCAGCGGC..... 1932
     ::::|||:::|||      ::::::   :::      :::|||
 168 yAlaAsnValThrValGlnArgSerThrIleValAspGlyGlyLeuHisI 185

1933 ..........AGACCAACACCGCACGCCTACAATCATTTAAACGACCAT 1971
               :::|||
 185 leGlyThrLeuGlnProLeu........................... 191

1972 TGGTCGCAAAAAGAGGGCATTCCTCGCGGGGAAATCGTGTGGGACAACGA 2021
        |||   |||   :::|||   :::::::::|||      :::
 192 ......GlnProGluAspLeuProProSerArgValValLeuGlyAspTh 206

2022 CTGGATCAAC.....................................CGCACAT 2038
       ::::::                                       :::|
 206 rSerValThrAlaValProAlaSerGlyAlaProAlaAlaValSerValP 223

2039 TTAAAGCGGAAAACTTCCAAATTAAAGGCGGACAGGCGGTGGTTTCCCGC 2088
     ||   |||:::::::::   :::   ||||||:::   :::   :::|||
 223 heGlyAlaAsnGluLeuThrValAspGlyGlyHisIleThrGlyGlyArg 239

2089 AATGTTGCCAAAGTGAAAGGCGATTGGCATTTGAGCAATCACGCCCAAGC 2138
       ::::::                                    :::   ||
 240 AlaAlaGly.....................................ValAlaAl 245

2139 AGTTTTTGGTGTCGCACCGCATCAAAGCCACACAATCTGTACACGTTCGG 2188
     |:::   |||:::      |||   :::::::::         |||:::|
 245 aMetAspGlyAlaIleValHisLeuGlnArgAlaThrIleArgArgGlyA 262

2189 AC.................................................. 2190
     ||
 262 spAlaProAlaGlyGlyAlaValProGlyGlyAlaValProGlyGlyPhe 278

2191 ..................TGGACGGGTCTGACAAATTGTGTCGAAAAAAC 2222
                        |||   |||:::
 279 GlyProLeuLeuAspGlyTrpTyrGlyVal..................... 288

2223 CATTACCGACGATAAAGTGATTGCTTCATTGACTAAGACCGACATCAGC. 2271
                                                |||:::|||
 289 .....................................AspValSerA 292

2272 ..GGCAATGTCGATCTTGCCGATCACGCTCATTTAAATCTCACAGGGCTT 2319
       ::::::|||||||||||||:::           :::::::::
 292 spSerThrValAspLeuAlaGln............SerIleValGluAla 304

2320 GCCACACTCAACGGCAATCTTAGTGCAAATGGCGATACACGTTATACAGT 2369
           |||::::::   :::   |||:::      :::|||   |||||
 305 ProGlnLeuGlyAlaAlaIleArgAlaGlyArgGlyAlaArgValThrVa 321

2370 CAGCCACAAC......GCCACCCAAAACGGCAACCTTAGCCTCGTGGGCA 2413
     ||||   :::      ::::::   :::|||||:::      :::||||:
 321 lSerGlyGlySerLeuSerAlaProHisGlyAsnValIleGluThrGlyG 338

2414 ATGCCCAAGCAACATTTAAT.................CAAGCCACATTA 2445
     :::::      |||                      :::   ||||||
 338 lyGlyAlaArgArgPheProProProAlaSerProLeuSerIleThrLeu 354

2446 AACGGCAACACATCGGCTTCGGGCAATGCT...TCATTTAATCTAAGCGA 2492
     ::::::::::::   |||:::|||:::|||      :::::::::
 355 GlnAlaGlyAlaArgAlaGlnGlyArgAlaLeuLeuTyrArgValLeuPr 371

2493 CCACGCCGTACAAAACGGCAGTCTGACGCTTTCCGGCAACGCTAAGGCAA 2542
       :::   |||:::         |||||||||:::|||:::|||::::::
 371 oGluProValLys.........LeuThrLeuAlaGlyGlyAlaGlnGly. 384

2543 ACGTAAGCCATTCCGCACTCAACGGTAATGTCTCCCTAGCCGATAAGGCA 2592
                          :::|||::::::      :::
 385 ...................GlnGlyAspIleValAlaThr......... 391

2593 GTATTCCATTTTGAAAGCAGCCGCTTTACCGGACAAATCAGCGGCGGCAA 2642
                     |||         :::   |||      ||||||
 392 ............GluLeuProProIleProGlyAlaSerSerGlyProLe 404

2643 GGATACGGCATTACACTTAAAAGACAGCGAATGGACGCTGCCGTCAGGCA 2692
       |||:::||||||      :::::::::::||||||      :::
 404 uAspValAlaLeu...AlaSerGlnAlaArgTrpThr...GlyAlaThrA 419

2693 CGGAATTAGGCAATTTAAACCTTGACAACGCCACCATTACACTCAATTCC 2742
           :::   :::|||:::::::||||||||||||   ::::::
 419 rgAlaValAspSerLeuSerIleAspAsnAlaThrTrpValMet...... 433

2743 GCCTATCGCCACGATGCGGCAGGGGCGCAAACCGGCAGTGCGACAGATGC 2792
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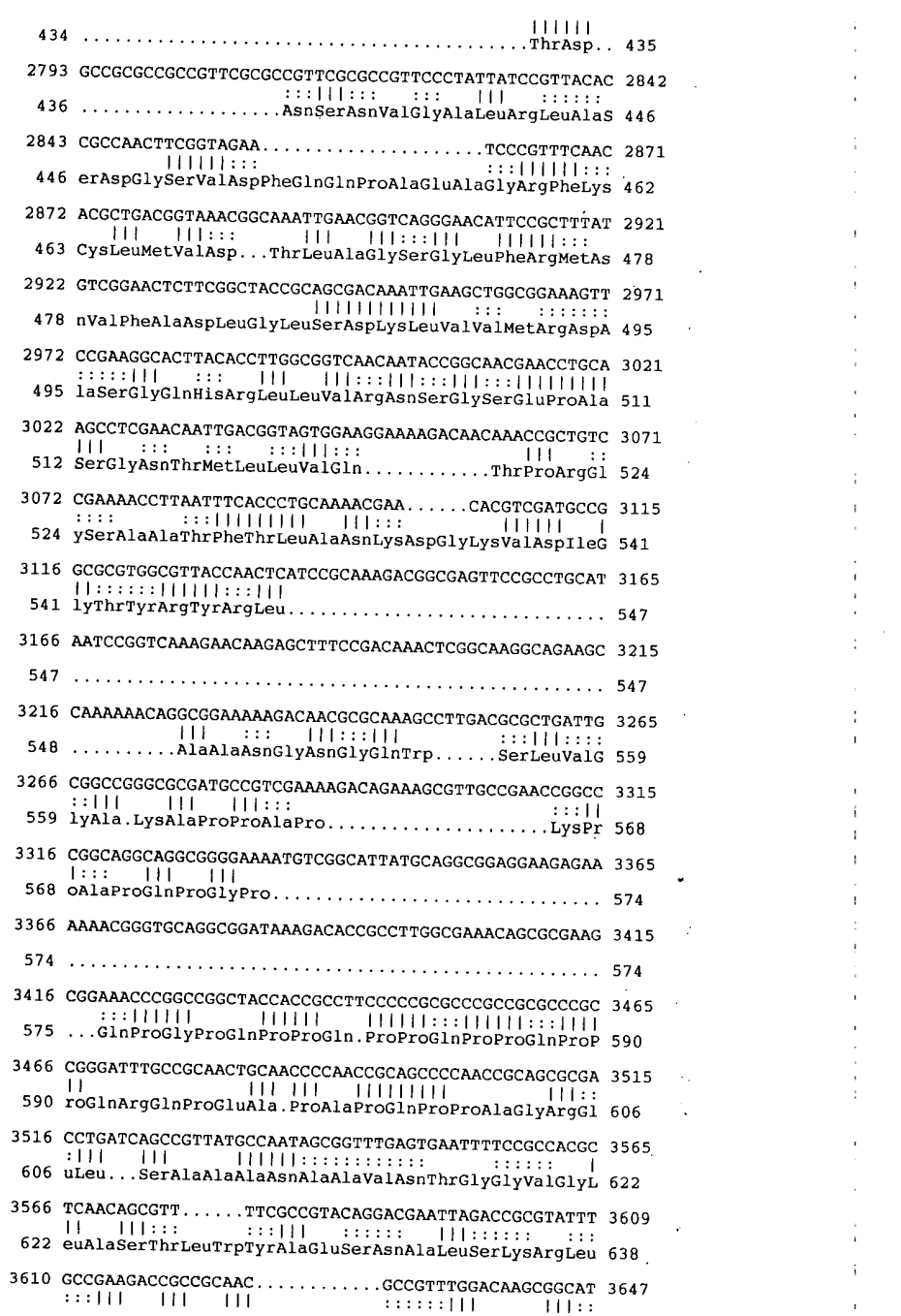

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seq_documentation_block:
ID AAR25578 standard; Protein; 922 AA.
XX
AC AAR25578;
XX

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DT   08-JAN-1993  (first entry)
XX
DE   Bordetella parapertussis P95 antigen precursor.
XX
KW   Whooping cough; P70 antigen; P95 precursor protein; vaccination.
XX
OS   Bordetella parapertussis.
XX
FH   Key             Location/Qualifiers
FT   Protein         35..643
FT                   /label= P70
FT   Binding-site    260..262
FT                   /note= "motif associated with cell-cell adhesion"
FT   Region          266..285
FT                   /note= "contains 5 direct, tandem repeats"
FT   Region          575..612
FT                   /note= "contains 9 direct repeats of Pro-Gln-Pro"
FT   Binding-site    712..714
FT                   /note= "motif associated with cell-cell adhesion"
XX
PN   WO9211292-A.
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PD   09-JUL-1992.
XX
PF   23-DEC-1991;   91WO-GB02302.
XX
PR   21-DEC-1990;   90GB-0027901.
XX
PA   (WELL ) WELLCOME FOUND LTD.
XX
PI   Charles IG;
XX
DR   WPI; 1992-250033/30.
DR   N-PSDB; AAQ26509.
XX
PT   Acellular vaccine for immunisation against whooping cough -
PT   comprises protein uncontaminated by B. para:pertussis components
PT   and capable of binding antibodies which bind native P70 antigen
XX
PS   Claim 1; Fig 1; 20pp; English.
XX
CC   A cosmid library was constructed by transforming E.coli HB101 with
CC   recombinant cosmids prepared by partial digestion of B.parapertussis
CC   chromosomal DNA with Sau3A and cloning of 40-50kb fragments into the
CC   BamHI site of cosmid pHC79. The cosmids were screened with a 1.8kb
CC   ClaI fragment from the prn gene of B.pertussis. The insert from one
CC   positive colony, harbouring cosmid pBD811, was sequenced and found to
CC   contain an open reading frame encoding a 922 amino acid protein
CC   with calculated mol.wt. 95,177. This precursor protein ("P95") is
CC   processed in vivo to the P70 antigen of apparent mol. wt. 70,000 as
CC   determined by SDS-PAGE, but with actual mol.wt. 61kD. Antigenic
CC   fragments of the protein will be useful in developing an acellular
CC   vaccine against B.parapertussis. Preferred fragments include amino
CC   acids Pro577 to Pro612 or Ala574 to Pro612.
XX
SQ   Sequence   922 AA;


alignment_scores:
            Quality:  295.00              Length:   1083
              Ratio:  0.602                Gaps:     52
 Percent Similarity:  45.245   Percent Identity: 22.253

alignment_block:
 US-09-303-518D-649 x AAR25578   ..

 Align seg 1/1  to: AAR25578  from: 1  to: 922

    1417 GGGGAAAACCAAGGCTCGATCAGCGTGGGCGACGGTACAGTCATTTTGGA 1466
         ||||||:::|||   :::|||   :::
      45 GlyGluArgGlnHisGlyIleHisIle..................... 53

    1467 TCAGCAGGCAGACGATAAAGGCAAAAAACAAGCCTTTAGTGAAATCGGCT 1516
```

```
         :::|||:::|||      |||   :::   |||   :::
  54 .LysGlnSerAspGlyAlaGlyValArgThrAlaThrGlyThrThrIleL 70

1517 TGGTCAGCGGCAGGGGTACGGTGCAACTGAATGCCGATAATCAGTTCAAC 1566
       ||||||||||||   :::      :::      :::|||
  70 ysValSerGlyArgGlnAlaGlnGlyValLeuLeuGluAsn..... 83

1567 CCCGACAAACTCTATTTCGGCTTTCGCGGCGGACGTTTGGATTTAAACGG 1616
                  :::   |||:::::::|||   :::      :::||
  84 ...ProAlaAlaGluLeuArgPheGlnAsnGlySerValThrSerSerGl 99

1617 GCATTCGCTTTCGTTCCACCGTATTCAAAATACCGATGAAGGGGCGATGA 1666
     |                          |||      |||||||||:::
  99 y.....................GlnLeuPheAspGluGlyVal.... 106

1667 TTGTCAACCACAATCAAGACAAAGAATCCACCGTTACCATTACAGGCAAT 1716
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 107 .............ArgArgPheLeuGlyThrValThrValLysAlaGly 118

1717 AAA.........GATATTGCTACAACCGGCAATAACAACAGCTTGGATAG 1757
     |||         |||   ||||||   :::|||
 119 LysLeuValAlaAspHisAlaThrLeuAlaAsn.................. 129

1758 CAAAAAAGAAATTGCCTACAACGGTTGGTTTGGCGAGAAAGATACGACCA 1807
                                        :::||||||
 130 ................................ValSerAspThrArgA 135

1808 AAACGAACGGGCGGCTCAACCTTGTT............TACCAGCCCGCC 1845
           ::|||            |||            |||   :::
 135 spAspAspGlyIleAlaLeuTyrValAlaGlyGluGlnAlaGlnAlaSer 151

1846 GCAGAAGACCGCACCCTGCTGCTTTCCGGCGGAACAAATTTA......AA 1889
           |||   ||||||      :::|||||:::::::::      ::
 152 IleAlaAspSerThrLeuGlnGlyAlaGlyGlyValArgValGluArgGl 168

1890 CGGCAACATCACGCAAACAAACGGCAAACTGTTTTTCAGCGGC....... 1932
     ::::|||:::|||      ::::::   :::      :::|||
 168 yAlaAsnValThrValGlnArgSerThrIleValAspGlyGlyLeuHisI 185

1933 ...........AGACCAACACCGCACGCCTACAATCATTTAAACGACCAT 1971
                 :::|||
 185 leGlyThrLeuGlnProLeu............................. 191

1972 TGGTCGCAAAAAGAGGGCATTCCTCGCGGGGAAATCGTGTGGGACAACGA 2021
           |||   |||   :::|||   :::::::::|||      :::
 192 ......GlnProGluAspLeuProProSerArgValValLeuGlyAspTh 206

2022 CTGGATCAACCGC.............................ACAT 2038
       ::::::                                  :::|
 206 rSerValThrAlaValProAlaSerGlyAlaProAlaAlaValPheValP 223

2039 TTAAAGCGGAAAACTTCCAAATTAAAGGCGGACAGGCGGTGGTTTCCCGC 2088
     ||   |||:::::::::   :::   ||||||:::   :::   :::|||
 223 heGlyAlaAsnGluLeuThrValAspGlyGlyHisIleThrGlyGlyArg 239

2089 AATGTTGCCAAAGTGAAAGGCGATTGGCATTTGAGCAATCACGCCCAAGC 2138
       ::::::                                  :::   ||
 240 AlaAlaGly..............................ValAlaAl 245

2139 AGTTTTTGGTGTCGCACCGCATCAAAGCCACACAATCTGTACACGTTCGG 2188
     |:::   |||:::      |||   :::::::::          |||:::|
 245 aMetAspGlyAlaIleValHisLeuGlnArgAlaThrIleArgArgGlyA 262

2189 AC.......................................... 2190
     ||
 262 spAlaProAlaGlyGlyAlaValProGlyGlyAlaValProGlyGlyAla 278

2191 ..............................TGGACGGGTCTGACAAA 2207
                                    |||   |||:::
 279 ValProGlyGlyPheGlyProLeuLeuAspGlyTrpTyrGlyVal..... 293

2208 TTGTGTCGAAAAAACCATTACCGACGATAAAGTGATTGCTTCATTGACTA 2257
```

```
 293 ..................................................  293

2258 AGACCGACATCAGC...GGCAATGTCGATCTTGCCGATCACGCTCATTTA 2304
      |||:::|||   ::::::||||||||||||||:::
 294 .....AspValSerAspSerThrValAspLeuAlaGln.............  304

2305 AATCTCACAGGGCTTGCCACACTCAACGGCAATCTTAGTGCAAATGGCGA 2354
     :::::::::          |||:::::::   :::   |||:::
 305 SerIleValGluAlaProGlnLeuGlyAlaAlaIleArgAlaGlyArgGl  321

2355 TACACGTTATACAGTCAGCCACAAC......GCCACCCAAAACGGCAACC 2398
      :::|||   |||||||||   :::      ::::::   :::|||||||:
 321 yAlaArgValThrValSerGlyGlySerLeuSerAlaProHisGlyAsnV  338

2399 TTAGCCTCGTGGGCAATGCCCAAGCAACATTTAAT.............. 2433
     ::      :::|||:::::          |||
 338 alIleGluThrGlyGlyGlyAlaArgArgPheProProProAlaSerPro  354

2434 ...CAAGCCACATTAAACGGCAACACATCGGCTTCGGGCAATGCT...TC 2477
        :::   |||||||:::::::::::::   |||:::|||:::|||
 355 LeuSerIleThrLeuGlnAlaGlyAlaArgAlaGlnGlyArgAlaLeuLe  371

2478 ATTTAATCTAAGCGACCACGCCGTACAAAACGGCAGTCTGACGCTTTCCG 2527
      :::::::::       :::   |||:::          |||||||||:::|
 371 uTyrArgValLeuProGluProValLys.........LeuThrLeuAlaG  385

2528 GCAACGCTAAGGCAAACGTAAGCCATTCCGCACTCAACGGTAATGTCTCC 2577
     ||:::|||::::::                        :::|||:::::
 385 lyGlyAlaGlnGly.....................GlnGlyAspIleVal  394

2578 CTAGCCGATAAGGCAGTATTCCATTTTGAAAGCAGCCGCTTTACCGGACA 2627
        :::                  |||          :::   |||
 395 AlaThr.....................GluLeuProProIleProGlyAl  404

2628 AATCAGCGGCGGCAAGGATACGGCATTACACTTAAAAGACAGCGAATGGA 2677
       ||||||      |||:::|||||||      :::::::::::::||||
 404 aSerSerGlyProLeuAspValAlaLeu...AlaSerGlnAlaArgTrpT  420

2678 CGCTGCCGTCAGGCACGGAATTAGGCAATTTAAACCTTGACAACGCCACC 2727
     ||      :::         :::   :::|||:::::::|||||||||||
 420 hr...GlyAlaThrArgAlaValAspSerLeuSerIleAspAsnAlaThr  435

2728 ATTACACTCAATTCCGCCTATCGCCACGATGCGGCAGGGGCGCAAACCGG 2777
       ::::::
 436 TrpValMet.....................................  438

2778 CAGTGCGACAGATGCGCCGCGCCGCCGTTCGCGCCGTTCGCGCCGTTCCC 2827
           ||||||                  :::|||:::   :::
 439 .......ThrAsp.....................AsnSerAsnValGlyA  446

2828 TATTATCCGTTACACCGCCAACTTCGGTAGAA.................. 2859
       |||   ::::::         ||||||:::
 446 laLeuArgLeuAlaSerAspGlySerValAspPheGlnGlnProAlaGlu  462

2860 ...TCCCGTTTCAACACGCTGACGGTAAACGGCAAATTGAACGGTCAGGG 2906
      :::|||||||:::::::|||   |||:::      |||   |||:::||
 463 AlaGlyArgPheLysValLeuMetValAsp...ThrLeuAlaGlySerGl  478

2907 AACATTCCGCTTTATGTCGGAACTCTTCGGCTACCGCAGCGACAAATTGA 2956
     |   ||||||:::                                |||||||||||
 478 yLeuPheArgMetAsnValPheAlaAspLeuGlyLeuSerAspLysLeuV  495

2957 AGCTGGCGGAAAGTTCCGAAGGCACTTACACCTTGGCGGTCAACAATACC 3006
       :::   :::::::::::::|||   :::   |||   |||:::|||:::
 495 alValMetArgAspAlaSerGlyGlnHisArgLeuTrpValArgAsnSer  511

3007 GGCAACGAACCTGCAAGCCTCGAACAATTGACGGTAGTGGAAGGAAAAGA 3056
     |||:::|||||||||||||   :::   :::   :::|||:::
 512 GlySerGluProAlaSerGlyAsnThrMetLeuLeuValGln........  525

3057 CAACAAACCGCTGTCCGAAAACCTTAATTTCACCCTGCAAAACGAA.... 3102
           |||   ::::::       :::|||||||||   |||:::
 526 ....ThrProArgGlySerAlaAlaThrPheThrLeuAlaAsnLysAspG  541

3103 ..CACGTCGATGCCGGCGCGTGGCGTTACCAACTCATCCGCAAAGACGGC 3150
           ||||||   |||:::::::||||||:::|||
 541 lyLysValAspIleGlyThrTyrArgTyrArgLeu.............. 552

3151 GAGTTCCGCCTGCATAATCCGGTCAAAGAACAAGAGCTTTCCGACAAACT 3200

 552 .................................................. 552

3201 CGGCAAGGCAGAAGCCAAAAAACAGGCGGAAAAAGACAACGCGCAAAGCC 3250
                                  |||   :::   |||:::|||
 553 ........................AlaAlaAsnGlyAsnGlyGlnTrp. 560

3251 TTGACGCGCTGATTGCGGCCGGGCGCGATGCCGTCGAAAAGACAGAAAGC 3300
           :::|||::::::|||    |||   |||:::         |||
 561 .....SerLeuValGlyAla.LysAlaProProAla......ProLysPr 573

3301 GTTGCCGAACCGGCCCGGCAGGCAGGCGGGGAAAATGTCGGCATTATGCA 3350
           |||   :::|||||||   |||   |||   :::
 573 oAlaPro...GlnProGlyProGlnProGlyProGln.............  584

3351 GGCGGAGGAAGAGAAAAAACGGGTGCAGGCGGATAAAGACACCGCCTTGG 3400
                                                |||||||
 585 .....................................ProPro...  586

3401 CGAAACAGCGCGAAGCGGAAACCCGGCCGGCTACCACCGCCTTCCCCCGC 3450
                                        ||||||   ||||||:
 587 ............................GlnProProGln.ProProG  593

3451 GCCCGCCGCGCCCGCCGGGATTTGCCGCAACTGCAACCCCAA........ 3492
     ::|||||||:::|||||| :::   ||||||   |||||||:::
 593 lnProProGlnProPro.GlnProProGlnArgGlnProGluAlaProAl  609

3493 .CCGCAGCCCCAACCGCAGCGCGACCTGATCAGCCGTTATGCCAATAGCG 3541
      |||||||||          |||:::|||   |||     ||||||:::
 609 aProGlnProProAlaGlyArgGluLeu...SerAlaAlaAlaAsnAlaA  625

3542 GTTTGAGTGAATTTTCCGCCACGCTCAACAGCGTT......TTCGCCGTA 3585
     ::::::::       ::::::   |||   |||:::      :::|||
 625 laValAsnThrGlyGlyValGlyLeuAlaSerThrLeuTrpTyrAlaGlu  641

3586 CAGGACGAATTAGACCGCGTATTTGCCGAAGACCGCCGCAAC........ 3627
     ::::::   |||:::::::   ::::::|||   |||   |||
 642 SerAsnAlaLeuSerLysArgLeuGlyGluLeuArgLeuAsnProAspAl  658

3628 ....GCCGTTTGGACAAGCGGCATCCGGGACACCAAACACTACCGTTCGC 3673
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3674 AAGATTTCCGCGCCTACCGCCAACAAACCGACCTGCGCCAAATCGGTATG 3723
     ::      |||   :::   |||:::::::          :::::::|||
 675 rgAlaGlyArgArgPheAspGlnLysValAlaGlyPheGluLeuGlyAla  691

3724 CAGAAAAACCTC............GGCAGCGGGCGCGTCGGCATCCTGTT 3761
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3762 TTCGCACAACCGGACCGAAAACACCTTC...GACGACGGCATCGGCAACT 3808
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3809 CGGCACGGCTTGCCCACGGCGCCGTTTTCGGGCAATACGGCATCGACAGG 3858
     ::       :::      |||:::                  :::   :::
 725 hrAspSerValHisValGlyGlyTyrAlaThrTyrIleAlaAsnSerGly  741

3859 TTCTACATCGGCATCAGCGCGGGCGCGGGTTTTAGCAGCGGCAGCCTT.. 3906
     |||||||:::      :::      |||:::      ::::::::::::
 742 PheTyrLeuAspAlaThrLeuArgAlaSerArgLeuGluAsnAspPheLy  758

3907 ..........TCAGACGGC......ATCGGAGGCAAAATCCGCCGCCGCG 3940
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 758 sValAlaGlySerAspGlyTyrAlaValLysGlyLysTyrArgThrHisG  775
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775 lyValGlyValSerLeuGluAlaGlyArgArgPheAlaHisAlaAspGly 791

3988 TTCGGCATCGAACCGCACATCGGCGCAACGCGCTATTTCGTCCAAAAAGC 4037
792 TrpPheLeuGluProGlnAlaGluLeuAlaValPheArgValGlyGlyGl 808

4038 GGATTACCGCTACGAAAAC...GTCAATATCGCCACCCCCGGCCTTGCAT 4084
808 yAlaTyrArgAlaAlaAsnGlyLeuArgValArgAspGluGlyGlySerS 825

4085 TCAACCGCTACCGCGCGGGCATTAAGGCAGATTATTCATTCAAACCGGCG 4134
825 erValLeuGlyArgLeuGlyLeuGluValGlyLysArgIleGluLeuAla 841

4135 CAACACATTTCCATCACGCCTTATTTGAGCCTGTCCTATACCGATGCCGC 4184
842 GlyGlyArgGlnValGlnProTyrIleLysAlaSerValLeuGlnGluPh 858

4185 TTCGGGCAAAGTCCGAACACGCGTCAATACCGCCGTATTGGCTCAGGATT 4234
858 eAspGlyAlaGlyThrValArgThrAsnGlyIleAlaHisArgThrGluL 875

4235 TCGGCAAAACCCGCAGTGCGGAATGGGGCGTAAACGCCGAAATCAAAGGT 4284
875 euArgGlyThrArg...AlaGluLeuGly..................... 883

4285 TTCACGCTGTCCCTCCACGCTGCCGCCGCCAAAGGCCCGCAACTGGAAGC 4334
884 ......LeuGlyMetAlaAlaAlaLeuGlyArgGlyHisSerLeuTyrAl 898

4335 G......CAACACAGCGCGGGCATCAAATTAGGCTACCGCTGG 4371
898 aSerTyrGluTyrSerLysGlyProLysLeuAlaMetProTrp 912
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seq_documentation_block:

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XX
AC AAR41732;
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DT 26-APR-1994 (first entry)
XX
DE High molecular weight protein 4 (HMW4).
XX
KW HMW; high molecular weight protein; virus; vaccine; influenza;
KW epitope; immunity; haemophilus influenzae.
XX
OS Haemophilus influenzae.
XX
PN WO9319090-A.
XX
PD 30-SEP-1993.
XX
PF 16-MAR-1993; 93WO-US02166.
XX
PR 16-MAR-1992; 92GB-0005704.
XX
PA (BARE/) BARENKAMP S J.
PA (INRM) INSERM INST NAT SANTE & RECH MEDICALE.
XX
PI Barenkamp SJ;
XX
DR WPI; 1993-320683/40.
DR N-PSDB; AAQ49511.
XX
PT High molecular weight surface proteins - of non-typeable
PT haemophilus which exhibit immunogenic properties
XX
PS Claim 6; Figure 10; 100pp; English.
XX
CC The isolation and purification of the high molecular weight protein
CC enables the identification of the major protective epitopes of the
CC protein by conventional epitope mapping. These epitopes can then be
CC synthesised using standard techniques and incorporated into fully
CC synthetic or recombinant vaccines.
XX
SQ Sequence 1529 AA;

alignment_scores:
Quality: 289.50 Length: 1196
Ratio: 0.497 Gaps: 61
Percent Similarity: 48.746 Percent Identity: 20.652

alignment_block:
US-09-303-518D-649 x AAR41732 ..

Align seg 1/1 to: AAR41732 from: 1 to: 1529

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339 GGCACATAACGGC.....GGCTATAACAACGTTGATTTTGGTGCGG 379
523 lAsnLysAspAspLysGlnPheArgPheAsnAsnValSerIleAsnGlyT 540

380 AAGGAAGAAATCCCGATCAACATCGTTTTACTTATAAAATTGTGAAACGG 429
540 hrGlyLysGly.....LeuLysPhe.....IleAlaAsnGln 550

430 AATAATTATAAAGCAGGGACTAAAGGCCATCCTTATGGCGGCGATTATCA 479
551 AsnAsnPheThr.....HisLysPheAspGlyGluIleAs 562

480 TATGCCGCGTTTGCATAAATTTGTCACAGATGCAGAACCTGTTGAAATGA 529
562 n..... 562

530 CCAGTTATATGGATGGGCGGAAATATATCGATCAAAATAATTACCCTGAC 579
563 .....IleSerGlyIleValThrIleAsnGlnThrThrLysLysAsp 576

580 CGTGTTCGTATTGGGGCAGGCAGGCAATATTGGCGATCTGATGAAGATGA 629
577 .....ValLysTyrTrpAsnAlaSerLysAspSe 586

630 GCCCAATAACCGCGAAAGT...TCATATCATATTGCAAGTGCGTATTCTT 676
586 rTyrTrpAsnValSerSerLeuThrLeuAsnThrValGlnLysPheThrP 603

677 GGCTC.....GTTGGTGGCAAT..... 693
603 heIleLysPheValAspSerGlySerAsnSerGlnAspLeuArgSerSer 619

694 ......ACCTTTGCACAA.....AATGGATCAGGTGGTGGCACA.. 726
620 ArgArgSerPheAlaGlyValHisPheAsnGlyIleGlyGlyLysThrAs 636

727 .GTCAACTTAGGTAGTGAA.....AAAATTAAACATAGC. 759
636 nPheAsnIleGlyAlaAsnAlaLysAlaLeuPheLysLeuLysProAsnA 653

760 .....CCATATGGTTTTTTACCA..... 777
653 laAlaThrAspProLysLysGluLeuProIleThrPheAsnAlaAsnIle 669

778 ......ACAGGAGGCTCATTTGGCGACAGTGGCTCACCAATGTTTATCTA 821
670 ThrAlaThrGlyAsnSer.....AspSerServalMetPheAspIl 683

822 TGATGCCCAAAAGCAAAAGTGGTTA.....ATTAATGGGGTAT 859
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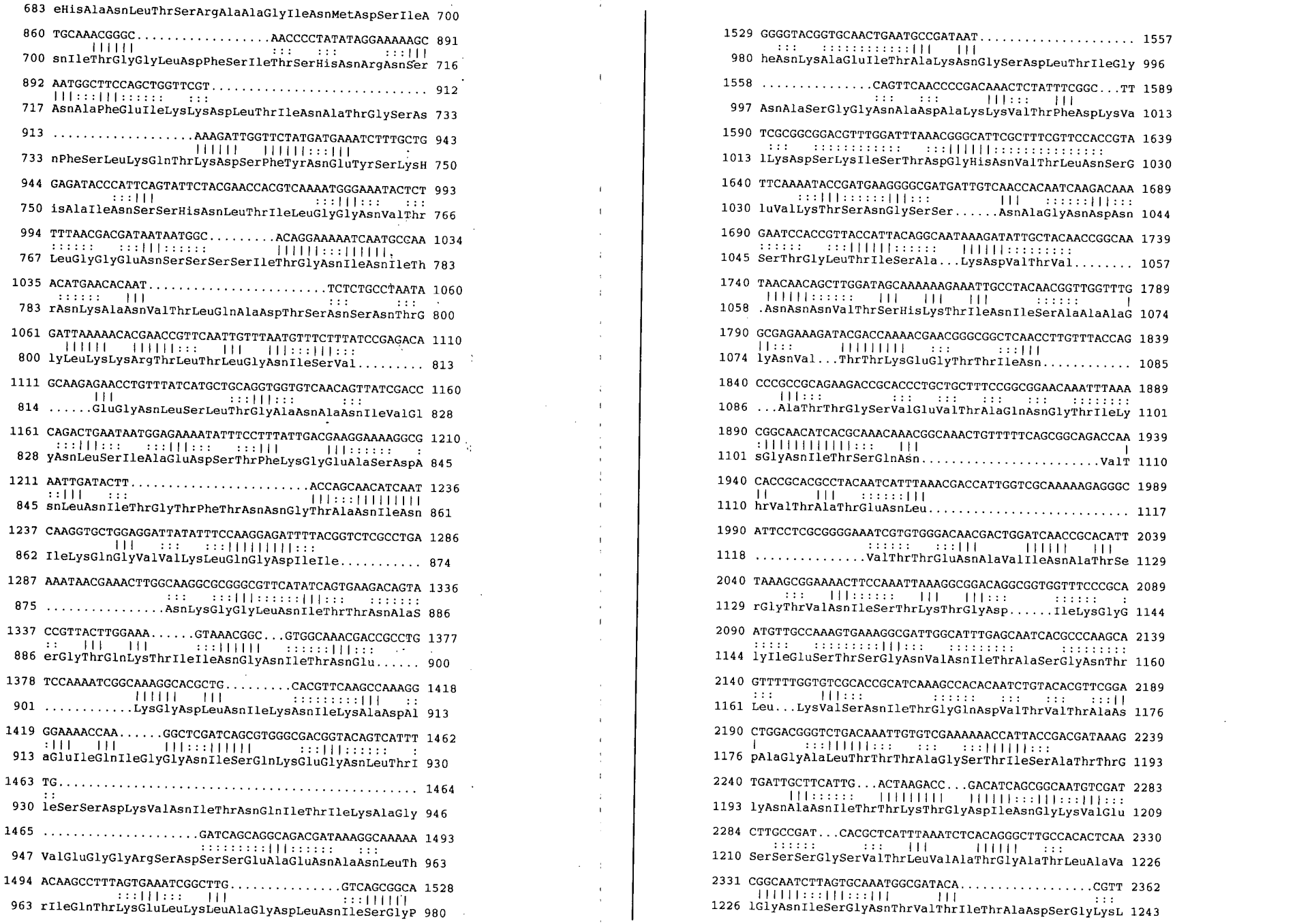

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 700 snIleThrGlyGlyLeuAspPheSerIleThrSerHisAsnArgAsnSer 716

 892 AATGGCTTCCAGCTGGTTCGT............................. 912
     |||:::|||:::::   :::
 717 AsnAlaPheGluIleLysLysAspLeuThrIleAsnAlaThrGlySerAs 733

 913 ...................AAAGATTGGTTCTATGATGAAATCTTTGCTG 943
                        ||||||   |||||||:::|||     :
 733 nPheSerLeuLysGlnThrLysAspSerPheTyrAsnGluTyrSerLysH 750

 944 GAGATACCCATTCAGTATTCTACGAACCACGTCAAAATGGGAAATACTCT 993
           :::|||                      :::|||:::   :::
 750 isAlaIleAsnSerSerHisAsnLeuThrIleLeuGlyGlyAsnValThr 766

 994 TTTAACGACGATAATAATGGC.........ACAGGAAAAATCAATGCCAA 1034
     ::::::   :::|||::::::          ||||||:::||||||
 767 LeuGlyGlyGluAsnSerSerSerSerIleThrGlyAsnIleAsnIleTh 783

1035 ACATGAACACAAT.......................TCTCTGCCTAATA 1060
      ::::::   |||                        :::     :::
 783 rAsnLysAlaAsnValThrLeuGlnAlaAspThrSerAsnSerAsnThrG 800

1061 GATTAAAAACACGAACCGTTCAATTGTTTAATGTTTCTTTATCCGAGACA 1110
       ||||||   ||||||:::   |||   |||:::|||:::
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1111 GCAAGAGAACCTGTTTATCATGCTGCAGGTGGTGTCAACAGTTATCGACC 1160
           |||                :::|||:::      :::
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1161 CAGACTGAATAATGGAGAAAATATTTCCTTTATTGACGAAGGAAAAGGCG 1210
      :::|||:::   :::|||:::   :::|||      |||::::::   :
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1211 AATTGATACTT.......................ACCAGCAACATCAAT 1236
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1237 CAAGGTGCTGGAGGATTATATTTCCAAGGAGATTTTACGGTCTCGCCTGA 1286
           |||   :::   :::|||||||||:::
 862 IleLysGlnGlyValValLysLeuGlnGlyAspIleIle........... 874

1287 AAATAACGAAACTTGGCAAGGCGCGGGCGTTCATATCAGTGAAGACAGTA 1336
                     :::   :::|||:::::|||:::   :::::::
 875 ................AsnLysGlyGlyLeuAsnIleThrThrAsnAlaS 886

1337 CCGTTACTTGGAAA......GTAAACGGC...GTGGCAAACGACCGCCTG 1377
      ::   |||   |||          :::||||||    ::::::|||:::
 886 erGlyThrGlnLysThrIleIleAsnGlyAsnIleThrAsnGlu...... 900

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                 ||||||   |||              ::::::::|||   ::
 901 ...........LysGlyAspLeuAsnIleLysAsnIleLysAlaAspAl 913

1419 GGAAAACCAA......GGCTCGATCAGCGTGGGCGACGGTACAGTCATTT 1462
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1463 TG......................................... 1464
     ::
 930 leSerSerAspLysValAsnIleThrAsnGlnIleThrIleLysAlaGly 946

1465 .....................GATCAGCAGGCAGACGATAAAGGCAAAAA 1493
                          ::::::::|||::::::   :::
 947 ValGluGlyGlyArgSerAspSerSerGluAlaGluAsnAlaAsnLeuTh 963

1494 ACAAGCCTTTAGTGAAATCGGCTTG..............GTCAGCGGCA 1528
           :::|||:::   |||                   :::||||||
 963 rIleGlnThrLysGluLeuLysLeuAlaGlyAspLeuAsnIleSerGlyP 980

1529 GGGGTACGGTGCAACTGAATGCCGATAAT..................... 1557
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1558 ...............CAGTTCAACCCCGACAAACTCTATTTCGGC...TT 1589
                    :::    :::       |||:::   |||
 997 AsnAlaSerGlyGlyAsnAlaAspAlaLysLysValThrPheAspLysVa 1013

1590 TCGCGGCGGACGTTTGGATTTAAACGGGCATTCGCTTTCGTTCCACCGTA 1639
      :::   ::::::::::::   :::||||||::::::::::::::::
1013 lLysAspSerLysIleSerThrAspGlyHisAsnValThrLeuAsnSerG 1030

1640 TTCAAAATACCGATGAAGGGGCGATGATTGTCAACCACAATCAAGACAAA 1689
          :::|||::::::|||:::         |||    ::::::|||:::
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1690 GAATCCACCGTTACCATTACAGGCAATAAAGATATTGCTACAACCGGCAA 1739
     ::::::   :::||||||::::::   ||||||::::::::
1045 SerThrGlyLeuThrIleSerAla...LysAspValThrVal........ 1057

1740 TAACAACAGCTTGGATAGCAAAAAAGAAATTGCCTACAACGGTTGGTTTG 1789
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1058 .AsnAsnAsnValThrSerHisLysThrIleAsnIleSerAlaAlaAlaG 1074

1790 GCGAGAAAGATACGACCAAAACGAACGGGCGGCTCAACCTTGTTTACCAG 1839
      ||:::      |||||||||   :::      :::|||
1074 lyAsnVal...ThrThrLysGluGlyThrThrIleAsn............ 1085

1840 CCCGCCGCAGAAGACCGCACCCTGCTGCTTTCCGGCGGAACAAATTTAAA 1889
        |||:::      :::   :::   :::   :::   ::::::::
1086 ...AlaThrThrGlySerValGluValThrAlaGlnAsnGlyThrIleLy 1101

1890 CGGCAACATCACGCAAACAAACGGCAAACTGTTTTTCAGCGGCAGACCAA 1939
     :||||||||||||:::   |||                          |
1101 sGlyAsnIleThrSerGlnAsn........................ValT 1110

1940 CACCGCACGCCTACAATCATTTAAACGACCATTGGTCGCAAAAAGAGGGC 1989
     ||     |||   ::::::|||
1110 hrValThrAlaThrGluAsnLeu........................... 1117

1990 ATTCCTCGCGGGGAAATCGTGTGGGACAACGACTGGATCAACCGCACATT 2039
                    ::::::   :::|||      ||||||   |||
1118 ...............ValThrThrGluAsnAlaValIleAsnAlaThrSe 1129

2040 TAAAGCGGAAAACTTCCAAATTAAAGGCGGACAGGCGGTGGTTTCCCGCA 2089
        :::   |||::::::   |||   |||:::      ::::::   :
1129 rGlyThrValAsnIleSerThrLysThrGlyAsp......IleLysGlyG 1144

2090 ATGTTGCCAAAGTGAAAGGCGATTGGCATTTGAGCAATCACGCCCAAGCA 2139
     ::::   :::::::::|||:::   :::::::::         :::::::::
1144 lyIleGluSerThrSerGlyAsnValAsnIleThrAlaSerGlyAsnThr 1160

2140 GTTTTTGGTGTCGCACCGCATCAAAGCCACACAATCTGTACACGTTCGGA 2189
     :::      |||:::            ::::::   :::   :::   :::||
1161 Leu...LysValSerAsnIleThrGlyGlnAspValThrValThrAlaAs 1176

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     |      :::||||||:::   :::   :::||||||:::
1176 pAlaGlyAlaLeuThrThrThrAlaGlySerThrIleSerAlaThrThrG 1193

2240 TGATTGCTTCATTG...ACTAAGACC...GACATCAGCGGCAATGTCGAT 2283
        |||::::::   |||||||||   ||||||:::|||:::|||:::
1193 lyAsnAlaAsnIleThrThrLysThrGlyAspIleAsnGlyLysValGlu 1209

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        ::::::      :::   |||      ||||||   :::
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2331 CGGCAATCTTAGTGCAAATGGCGATACA..................CGTT 2362
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1226 lGlyAsnIleSerGlyAsnThrValThrIleThrAlaAspSerGlyLysL 1243
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2413 AATGCCCAAGCAACATTTAATCAAGCCACATTAAACGGCAACACATCGGC 2462
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1306 yLysLeuThrThrGlnThrGlySerSerIleThrSerSerAsnGlyGlnT 1323

2648 CGGCATTACACTTAAAAGACAGCGAATGGACGCTGCCGTCAGGCACGGAA 2697
1323 hrThrLeuThrAlaLysAspSer...................SerIle 1332

2698 TTAGGCAATTTAAACCTTGACAACGCCACCATTACACTCAATTCCGCCTA 2747
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2748 TCGCCACGATGCGGCAGGGGCGCAAACCGGCAGTGCGACAGATGCGCCGC 2797
1346 .....................ThrGlyThr.............,... 1348

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1349 ............................LeuThrThrThrGlyAsp 1354

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1355 SerLysIleAsnAlaThrSerGlyThrLeuThrIleAsnAlaLys..... 1369

2898 CGGTCAGGGAACATTCCGCTTTATGTCGGAACTCTTCGGCTACCGCAGCG 2947
1370 ..........................................AspA 1371

2948 ACAAATTGAAGCTGGCGGAAAGTTCCGAAGGCACTTACACCTTGGCGGTC 2997
1371 laLysLeuAspGlyAlaAlaSerGlyAspArgThrValValAsnAlaThr 1387

2998 AACAATACCGGCAACGAACCTGCAAGCCTCGAACAATTGACGGTAGTGGA 3047
1388 AsnAlaSerGlySer................................ 1392

3048 AGGAAAAGACAACAAACCGCTGTCCGAAAACCTTAATTTCACCCTGCAAA 3097
1393 .GlyAsnValThrAlaLysThrSerSerSerValAsnIleThrGlyAspL 1409

3098 ACGAACACGTCGATGCCGGCGCGTGGCGTTACCAACTCATCCGCAAAGAC 3147
1409 euAsnThrIleAsnGly............LeuAsnIleIleSerGluAsn 1421

3148 GGCGAGTTCCGCCTGCATAATCCGGTCAAAGAACAAGAGCTTTCCGACAA 3197
1422 Gly............ArgAsnThrVal...................Ar 1427

3198 ACTCGGCAAGGCAGAAGCCAAAAAACAGGCGGAAAAAGACAACGCGCAAA 3247
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3248 GCCTTGACGCGCTGATTGCGGCCGGGCGCGATGCCGTCGAAAAGACAGAA 3297
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3298 AGCGTTGCCGAACCGGCCCGGCAGGCAGGCGGGGAAAATGTCGGCATTAT 3347
1460 AspLeuSerAspGluGluArgGluThrLeuAlaLys...LeuGlyValSe 1475

3348 GCAGGCGGAGGAAGAGAAAAAACGGGTGCAGGCGGATAAAGACACCGCCT 3397
1475 rAlaVal.............ArgPheValGluProAsnAsnAlaIleThrV 1488

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1488 alAsnThrGlnAsnGluPheThrThrLysProSerSer 1500
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seq_documentation_block:

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AC   AAW30292;
XX
DT   14-APR-1998  (first entry)
XX
DE   Non-typeable Haemophilus high mol.wt. surface protein HMW4.
XX
KW   Non-typeable Haemophilus; high molecular weight surface protein;
KW   HMW4; immunogen; vaccine; otitis media.
XX
OS   Haemophilus influenzae strain 5.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 372
FT                   /note= "encoded by TCT"
FT   Misc-difference 400
FT                   /note= "encoded by AAT"
XX
PN   WO9736914-A1.
XX
PD   09-OCT-1997.
XX
PF   01-APR-1997;   97WO-US04707.
XX
PR   01-APR-1996;   96US-0617697.
XX
PA   (BARE/) BARENKAMP S J.
XX
PI   Barenkamp SJ;
XX
DR   WPI; 1997-503038/46.
DR   N-PSDB; AAT90993.
XX
PT   High molecular weight proteins of non-typeable Haemophilus
PT   influenzae - useful for vaccine production
XX
PS   Claim 1; Page 97-102; 183pp; English.
XX
CC   This protein comprises the high molecular weight surface protein
CC   HMW4 (123 kDa) of non-typeable Haemophilus influenzae strain 5 that
CC   has the immunological ability to protect against disease caused by
CC   a non-typeable Haemophilus strain and is characterised by at least
CC   one surface-exposed B-cell epitope that is recognised by monoclonal
CC   antibody AD6.  The HMW4 amino acid sequence was deduced from an
CC   isolated hmw4 gene (see AAT90993).  HMW1 (see AAW30293), HMW2 (see
CC   AAW30294) and HMW3 (see AAW30291) have also been identified.  A
CC   conjugate comprising HMW4 linked to an antigen, hapten or
CC   polysaccharide, and a synthetic peptide of 6-150 amino acids
CC   corresponding to at least protective epitope of HMW4 are also
CC   claimed.  HMW proteins, conjugates and peptides can be used in
CC   vaccines, as immunogens for preparation of antibodies and as
CC   antigens for detection of these antibodies.
XX
SQ   Sequence   1601 AA;
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           Quality:  286.50              Length:   1189
             Ratio:  0.491                Gaps:       64
 Percent Similarity:  49.117   Percent Identity: 21.026

alignment_block:
 US-09-303-518D-649 x AAW30292   ..

 Align seg 1/1  to: AAW30292  from: 1  to: 1601

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     579 AlaArgAsnAlaThrAspAlaGlnIleThrAlaGlnGlyThrIleThrVa 595

     339 GGCACATAACGGC.........GGCTATAACAACGTTGATTTTGGTGCGG 379
         |   :::                :::||||||||||:::::::::::
     595 lAsnLysAspAspLysGlnPheArgPheAsnAsnValSerIleAsnGlyT 612

     380 AAGGAAGAAATCCCGATCAACATCGTTTTACTTATAAAATTGTGAAACGG 429
         |||::::::          :::|||         |||:::::::::
     612 hrGlyLysGly.........LeuLysPhe.........IleAlaAsnGln 622

     430 AATAATTATAAAGCAGGGACTAAAGGCCATCCTTATGGCGGCGATTATCA 479
         ||||||:::                |||   :::   |||:::   ::
     623 AsnAsnPheThr..............HisLysPheAspGlyGluIleAs 634

     480 TATGCCGCGTTTGCATAAATTTGTCACAGATGCAGAACCTGTTGAAATGA 529
         :
     634 n..................................................  634

     530 CCAGTTATATGGATGGGCGGAAATATATCGATCAAAATAATTACCCTGAC 579
               ::::::|||          |||:::|||::::::      |||
     635 ........IleSerGlyIleValThrIleAsnGlnThrThrLysLysAsp 648

     580 CGTGTTCGTATTGGGGCAGGCAGGCAATATTGGCGATCTGATGAAGATGA 629
                          :::||||||:::::::::::::|||::
     649 .....................ValLysTyrTrpAsnAlaSerLysAspSe 658

     630 GCCCAATAACCGCGAAAGT...TCATATCATATTGCAAGTGCGTATTCTT 676
         :     |||   :::|||   :::   :::   ::::::   :::::::
     658 rTyrTrpAsnValSerSerLeuThrLeuAsnThrValGlnLysPheThrP 675

     677 GGCTC............GTTGGTGGCAAT..................... 693
         :::::               |||:::|||
     675 heIleLysPheValAspSerGlySerAsnSerGlnAspLeuArgSerSer 691

     694 ......ACCTTTGCACAA.........AATGGATCAGGTGGTGGCACA.. 726
               :::||||||           ||||||   ||||||   |||
     692 ArgArgSerPheAlaGlyValHisPheAsnGlyIleGlyGlyLysThrAs 708

     727 .GTCAACTTAGGTAGTGAA..............AAAATTAAACATAGC. 759
         |||:::|||::::::                 |||:::|||   :::
     708 nPheAsnIleGlyAlaAsnAlaLysAlaLeuPheLysLeuLysProAsnA 725

     760 ...........CCATATGGTTTTTTACCA..................... 777
                    |||         ||||||
     725 laAlaThrAspProLysLysGluLeuProIleThrPheAsnAlaAsnIle 741

     778 ......ACAGGAGGCTCATTTGGCGACAGTGGCTCACCAATGTTTATCTA 821
               ||||||:::|||          :::::::|||   ||||||
     742 ThrAlaThrGlyAsnSer.........AspSerSerValMetPheAspIl 755

     822 TGATGCCCAAAAGCAAAAGTGGTTA............ATTAATGGGGTAT 859
             |||:::      :::                  ::::::::::::
     755 eHisAlaAsnLeuThrSerArgAlaAlaGlyIleAsnMetAspSerIleA 772

     860 TGCAAACGGGC.................AACCCCTATATAGGAAAAAGC 891
               ||||||                 :::   :::      :::|||
     772 snIleThrGlyGlyLeuAspPheSerIleThrSerHisAsnArgAsnSer 788

     892 AATGGCTTCCAGCTGGTTCGT.......................... 912

         |||:::|||::::::   :::
     789 AsnAlaPheGluIleLysLysAspLeuThrIleAsnAlaThrGlySerAs 805

     913 ...................AAAGATTGGTTCTATGATGAAATCTTTGCTG 943
                             ||||||   ||||||:::|||
     805 nPheSerLeuLysGlnThrLysAspSerPheTyrAsnGluTyrSerLysH 822

     944 GAGATACCCATTCAGTATTCTACGAACCACGTCAAAATGGGAAATACTCT 993
               :::|||                        :::|||:::   :::
     822 isAlaIleAsnSerSerHisAsnLeuThrIleLeuGlyGlyAsnValThr 838

     994 TTTAACGACGATAATAATGGC.........ACAGGAAAAATCAATGCCAA 1034
         ::::::   :::|||::::::         ||||||:::||||||
     839 LeuGlyGlyGluAsnSerSerSerSerIleThrGlyAsnIleAsnIleTh 855

    1035 ACATGAACACAAT.......................TCTCTGCCTAATA 1060
          ::::::   |||                      :::      :::
     855 rAsnLysAlaAsnValThrLeuGlnAlaAspThrSerAsnSerAsnThrG 872

    1061 GATTAAAAACACGAACCGTTCAATTGTTTAATGTTTCTTTATCCGAGACA 1110
           ||||||   ||||||:::   |||   |||:::|||:::
     872 lyLeuLysLysArgThrLeuThrLeuGlyAsnIleSerVal......... 885

    1111 GCAAGAGAACCTGTTTATCATGCTGCAGGTGGTGTCAACAGTTATCGACC 1160
               |||                 :::|||:::      :::
     886 ......GluGlyAsnLeuSerLeuThrGlyAlaAsnAlaAsnIleValGl 900

    1161 CAGACTGAATAATGGAGAAAATATTTCCTTTATTGACGAAGGAAAAGGCG 1210
          :::|||:::   :::|||:::   :::|||      |||::::::   :
     900 yAsnLeuSerIleAlaGluAspSerThrPheLysGlyGluAlaSerAspA 917

    1211 AATTGATACTT.......................ACCAGCAACATCAAT 1236
         ::|||   :::                       |||:::||||||||
     917 snLeuAsnIleThrGlyThrPheThrAsnAsnGlyThrAlaAsnIleAsn 933

    1237 CAAGGTGCTGGAGGATTATATTTCCAAGGAGATTTTACGGTCTCGCCTGA 1286
               |||   :::   :::|||||||||:::
     934 IleLysGlnGlyValValLysLeuGlnGlyAspIleIle........... 946

    1287 AAATAACGAAACTTGGCAAGGCGCGGGCGTTCATATCAGTGAAGACAGTA 1336
                         :::   :::|||:::::::|||:::   :::::::
     947 ................AsnLysGlyGlyLeuAsnIleThrThrAsnAlaS 958

    1337 CCGTTACTTGGAAA......GTAAACGGC...GTGGCAAACGACCGCCTG 1377
         ::   |||   |||       :::|||||   ::::::|||:::
     958 erGlyThrGlnLysThrIleIleAsnGlyAsnIleThrAsnGlu...... 972

    1378 TCCAAAATCGGCAAAGGCACGCTG.........CACGTTCAAGCCAAAGG 1418
                   ||||||   |||          :::::::::|||   ::
     973 ............LysGlyAspLeuAsnIleLysAsnIleLysAlaAspAl 985

    1419 GGAAAACCAA......GGCTCGATCAGCGTGGGCGACGGTACAGTCATTT 1462
         :|||   |||       |||:::||||||      :::|||::::::   :
     985 aGluIleGlnIleGlyGlyAsnIleSerGlnLysGluGlyAsnLeuThrI 1002

    1463 TGGATCAGCAGGCAGACGATAAAGGCAAA......AAACAAGCCTTTAGT 1506
         ::          ::::::||||||   :::      :::|||
    1002 le.........SerSerAspLysValAsnIleThrAsnGlnIleThrIle 1015

    1507 GAAATCGGCTTGGTCAGCGGCAGGGGT...................... 1533
         :::   |||:::   :::|||||||:::
    1016 LysAlaGlyValGluGlyGlyArgSerAspSerSerGluAlaGluAsnAl 1032

    1534 .......ACGGTGCAACTGAATGCCGATAATCAGTTCAACCCCGACAAAC 1576
                |||:::|||   :::  ::::   ::::::      |||
    1032 aAsnLeuThrIleGln...ThrLysGluLeuLysLeuAlaGlyAspLeuA 1048

    1577 TCTATTTCGGCTTTCGCGGCGGACGTTTGGATTTA...AACGGGCATTCG 1623
               ||||||:::   :::::::::          ||||||   :::
    1048 snIleSerGlyPheAsnLysAlaGluIleThrAlaLysAsnGlySerAsp 1064

    1624 CTTTCGTTCCACCGTATTCAAAATACCGATGAAGGGGCGATGATTGTCAA 1673
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1065 LeuThrIleGlyAsnAlaSerGlyGlyAsnAlaAspAlaLysLysValTh 1081

1674 CCACAATCAAGACAAAGAATCCACCGTTACC.............ATTA 1708
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1709 CAGGCAATAAAGATATTGCTACAACC.................GGCAAT 1740
     ||  |||:::::::::  |||:::                  ||||||
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1741 AACAACAGCTTGGAT.........AGCAAAAAAGAAATTGCCTACAACGG 1781
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1131 ...............AsnIleValThrSerHisLysThrIleAsnIle. 1141

1832 TTTACCAGCCCGCCGCAGAAGACCGCACCCTGCTGCTTTCCGGCGGAACA 1881
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     ::::::|||:::                ::::::|||      ||||||
1155 ThrIleAsnAlaThrThrGlySerValGluValThrAlaGlnAsnGlyTh 1171

1917 ACTGTTTTTCAGCGGCAGACCAACACCGCACGCCTACAATCATTTAAACG 1966
      :::      :::|||:::  |||
1171 rIle......LysGlyAsnIleThr..................... 1177

1967 ACCATTGGTCGCAAAAAGAGGGCATTCCTCGCGGGGAA......ATCGTG 2010
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1178 ........SerGlnAsnValThrValThrAlaThrGluAsnLeuValThr 1191

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1192 ThrGluAsnAlaValIleAsnAlaThrSerGlyThrValAsnIleSerTh 1208

2061 TAAAGGCGGACAGGCGGTGGTTTCCCGCAATGTTGCCAAAGTGAAAGGCG 2110
      |||  |||:::     ::::::  ::::::  :::::::::|||:
1208 rLysThrGlyAsp......IleLysGlyGlyIleGluSerThrSerGlyA 1223

2111 ATTGGCATTTGAGCAATCACGCCCAAGCAGTTTTTGGTGTCGCACCGCAT 2160
     ::  :::::::::     ::::::::::::     |||:::
1223 snValAsnIleThrAlaSerGlyAsnThrLeu...LysValSerAsnIle 1238

2161 CAAAGCCACACAATCTGTACACGTTCGGACTGGACGGGTCTGACAAATTG 2210
       ::::::  :::  :::  :::|||      :::|||||:::
1239 ThrGlyGlnAspValThrValThrAlaAspAlaGlyAlaLeuThrThrTh 1255

2211 TGTCGAAAAAACCATTACCGACGATAAAGTGATTGCTTCATTG...ACTA 2257
      :::  :::|||||||:::                |||::::::  ||||
1255 rAlaGlySerThrIleSerAlaThrThrGlyAsnAlaAsnIleThrThrL 1272

2258 AGACC...GACATCAGCGGCAATGTCGATCTTGCCGAT...CACGCTCAT 2301
     |||||  ||||||:::|||:::|||:::  ::::::     :::
1272 ysThrGlyAspIleAsnGlyLysValGluSerSerSerGlySerValThr 1288

2302 TTAAATCTCACAGGGCTTGCCACACTCAACGGCAATCTTAGTGCAAATGG 2351
     |||      ||||||  :::         ||||||:::|||:::|||
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2352 CGATACA.................CGTTATACAGTCAGCCACAACGCCA 2383
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1305 rValThrIleThrAlaAspSerGlyLysLeuThrSerThrValGlySerT 1322

2384 CCCAAAACGGCAACCTTAGCCTCGTGGGCAATGCCCAAGCAACATTTAAT 2433
     ||  ||||||:::  |||:::::::  :::::::|||:::
1322 hrIleAsnGlyThrAsnSerValThrThrSerSerGlnSerGlyAspIle 1338

2434 CAAGCCACATTAAACGGCAACACATCGGCTTCGGGCAATGCTTCATTTAA 2483
     ::::::|||::::::|||||||||                    ||
1339 GluGlyThrIleSerGlyAsnThr.....................ValAs 1348
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2484 TCTAAGCGACCACGCCGTACAAAACGGCAGTCTGACGCTTTCCGGCAACG 2533
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2534 CTAAGGCAAACGTAAGCCATTCCGCACTCAACGGTAATGTCTCCCTAGCC 2583
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2584 GATAAGGCAGTATTCCATTTTGAAAGCAGCCGCTTTACCGGACAA..... 2628
           |||::::::      ||||||:::::::::|||   |||
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2629 ..........ATCAGCGGCGGCAAGGATACGGCATTACACTTAAAAGACA 2668
                    |||::::::   :::|||:::|||      |||||||
1385 ySerSerIleThrSerSerAsnGlyGlnThrThrLeuThrAlaLysAspS 1402

2669 GCGAATGGACGCTGCCGTCAGGCACGGAATTAGGCAATTTAAACCTTGAC 2718
     ||                        :::      ||||||:::|||
1402 er....................SerIleAlaGlyAsnIleAsnAla... 1410

2719 AACGCCACCATTACACTCAATTCCGCCTATCGCCACGATGCGGCAGGGGC 2768
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1411 ...AlaAsnValThrLeuAsnThr........................... 1417

2769 GCAAACCGGCAGTGCGACAGATGCGCCGCGCCGCCGTTCGCGCCGTTCGC 2818
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2819 GCCGTTCCCTATTATCCGTTACACCGCCAACTTCGGTAGAATCCCGTTTC 2868
                  |||::::::|||      :::::::::::::::
1421 ...........LeuThrThrThrGlyAspSerLysIleAsnAlaThrSer 1433

2869 AACACGCTGACGGTAAACGGCAAATTGAACGGTCAGGGAACATTCCGCTT 2918
     :::||||||||||:::|||:::|||
1434 GlyThrLeuThrIleAsnAlaLys.......................... 1441

2919 TATGTCGGAACTCTTCGGCTACCGCAGCGACAAATTGAAGCTGGCGGAAA 2968
                                    :::  ||||||      |||  |
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2969 GTTCCGAAGGCACTTACACCTTGGCGGTCAACAATACCGGCAACGAACCT 3018
     ||:::::::  |||  :::  |||:::|||  :::|||:::
1450 erGlyAspArgThrValValAsnAlaThrAsnAlaSerGlySer...... 1464

3019 GCAAGCCTCGAACAATTGACGGTAGTGGAAGGAAAAGACAACAAACCGCT 3068
                                       |||:::  :::
1465 ............................GlyAsnValThrAlaLysTh 1471

3069 GTCCGAAAACCTTAATTTCACCCTGCAAAACGAACACGTCGATGCCGGCG 3118
      |||::::::::::|||:::|||  :::  :::  :::::::::
1471 rSerSerSerValAsnIleThrGlyAspLeuAsnThrIleAsnGly.... 1486

3119 CGTGGCGTTACCAACTCATCCGCAAAGACGGCGAGTTCCGCCTGCATAAT 3168
                  ::::::|||  :::::::|||            :::|||
1487 ........LeuAsnIleIleSerGluAsnGly............ArgAsn 1496

3169 CCGGTCAAAGAACAAGAGCTTTCCGACAAACTCGGCAAGGCAGAAGCCAA 3218
        |||                  :::|||         |||
1497 ThrVal....................ArgLeuArgGlyLysGluIleAs 1506

3219 AAAACAGGCGGAAAAAGACAACGCGCAAAGCCTTGACGCGCTGATTGCGG 3268
        :::      :::  ::::::  |||::::::  :::|||  |
1506 pValLysTyrIleGlnProGlyValAlaSerValGluGluValIleGluA 1523

3269 CCGGGCGCGATGCCGTCGAAAAGACAGAAAGCGTTGCCGAACCGGCCCGG 3318
     ||  |||  ::::::||||||:::::::::::::::::::      |||
1523 laLysArg...ValLeuGluLysValLysAspLeuSerAspGluGluArg 1538

3319 CAGGCAGGCGGGGAAAATGTCGGCATTATGCAGGCGGAGGAAGAGAAAAA 3368
     ::::::  ::::::  :::|||:::      :::          ::
1539 GluThrLeuAlaLys...LeuGlyValSerAlaVal...........Ar 1550
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     3369 ACGGGTGCAGGCGGATAAAGACACCGCCTTGGCGAAACAGCGCGAAGCGG 3418
          :   |||:::   ::::::      ::::::      |||:::|||
     1550 gPheValGluProAsnAsnAlaIleThrValAsnThrGlnAsnGluPheT 1567

     3419 AAACCCGGCCGGCTACC 3435
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     1567 hrThrLysProSerSer 1572

seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1994.DAT:AAR63506

seq_documentation_block:
ID   AAR63506 standard; Protein; 1477 AA.
XX
AC   AAR63506;
XX
DT   25-JUN-1995  (first entry)
XX
DE   Haemophilus high molecular weight protein HMW2.
XX
KW   High molecular weight protein; HMW2; protective vaccine; otitis;
KW   sinusitis; bronchitis; Hib; ss.
XX
OS   Haemophilus.
XX
PN   WO9421290-A.
XX
PD   29-SEP-1994.
XX
PF   15-MAR-1994;   94WO-US02550.
XX
PR   16-MAR-1993;   93US-0038682.
XX
PA   (BARE/) BARENKAMP S J.
PA   (SGEM/) ST GEME J W.
XX
PI   Barenkamp SJ,  St GEME JW;
XX
DR   WPI; 1994-316665/39.
DR   Q-PSDB; Q72294.
XX
PT   New immunogenic high mol. wt. proteins of non typeable
PT   Haemophilus - useful in protective vaccines
XX
PS    Claim 3; Page 36; 127pp; English.
XX
CC   The HMW2 protein encoded by this sequence is useful in a vaccine to
CC   protect against disease caused by non-typeable Haemophilus which are
CC   not controlled by H. influenzae type b (Hib) vaccines.  The encoded
CC   protein can also be used as a carrier for protective Hib
CC   polysaccharide (in a conjugate vaccin against meningitis) or for
CC   other antigens, haptens, etc.
XX
SQ   Sequence   1477 AA;


alignment_scores:
           Quality:  287.00              Length:   1437
             Ratio:  0.415                Gaps:     66
 Percent Similarity:  48.156   Percent Identity: 19.415

alignment_block:
 US-09-303-518D-649 x AAR63506   ..

 Align seg 1/1  to: AAR63506  from: 1  to: 1477

     163 CGCGACTTTGCCGAAAATAAAGGCAAGTTTGCAGTCGGGGCGAAAGATAT 212
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     158 LysAspAlaIleIleAsnThrAsnGlyPheThrAlaSerThrLeuAspIl 174

     213 TGAGGTTTACAACAAAAAAGGGGAGTTGGTCGGCAAATCAATGACAAAA. 261
         |:::      |||   |||:::::::              ::::::||||||    .
     174 eSerAsnGluAsnIleLysAlaArgAsnPheThrPheGluGlnThrLysA 191

     262 ..........GCCCCGATGATTGATTTTTCTGTG......GTGTCGCGT 294
                    |||   :::::::::   ::::::      |||::::::
     191 spLysAlaLeuAlaGluIleValAsnHisGlyLeuIleThrValGlyLys 207

     295 AACGGCGTGGCGGCATTGGTGGGC............GATCAATATATTGT 332
         :::|||   :::   |||:::|||            ::::::   :::::
     208 AspGlySerValAsnLeuIleGlyGlyLysValLysAsnGluGlyValIl 224

     333 GAGCGTGGCACATAACGGCGGCTATAACAACGTTGATTTTGGT....... 375
         :||||||      |||||||||      ::::::      |||
     224 eSerVal......AsnGlyGlySerIleSerLeuLeuAlaGlyGlnLysI 239

     376 ........GCGGAAGGAAGAAATCCCGATCAACATCGTTTTACTTATAAA 417
                 ::::::      ||||||            :::||||||:::
     239 leThrIleSerAspIleIleAsnPro.........ThrIleThrTyrSer 252

     418 ATTGTGAAACGGAATAATTATAAAGCAGGGACTAAAGGCCATCCTTAT.. 465
         |||:::      :::|||   :::|||   :::   |||      :::
     253 IleAlaAlaProGluAsn...GluAlaValAsnLeuGlyAspIlePheAl 268

     466 ....GGCGGCGATTATCATATGCCGCGTTTGCATAAATTTGTCACAGATG 511
             ||||||:::   :::
     268 aLysGlyGlyAsnIleAsn............................... 274

     512 CAGAACCTGTTGAAATGACCAGTTATATGGATGGGCGGAAATATATCGAT 561

     274 ................................................... 274

     562 CAAAATAATTACCCTGACCGTGTTCGTATTGGGGCAGGCAGGCAATATTG 611
                              ||||||   ::::::   |||:::
     275 .....................ValArgAlaAlaThrIleArgAsnGlnGl 284

     612 GCGATCTGATGAAGATGAGCCCAATAACCGCGAAAGTTCATATCATATTG 661
          :::   :::   |||:::   ::::::   :::|||:::      :::
     284 yLysLeuSerAlaAspSerValSerLysAspLysSerGlyAsnIleValL 301

     662 CAAGTGCGTATTCTTGG......CTCGTTGGTGGCAATACCTTTGCACAA 705
           ||||||   :::            :::||||||         ||||||
     301 euSerAlaLysGluGlyGluAlaGluIleGlyGlyValIleSerAlaGln 317

     706 AAT..................................................... 708
         |||
     318 AsnGlnGlnAlaLysGlyGlyLysLeuMetIleThrGlyAspLysValTh 334

     709 ............................GGATCAGGTGGTGGCACAG 727
                                    |||:::   ||||||   :
     334 rLeuLysThrGlyAlaValIleAspLeuSerGlyLysGluGlyGlyGluT 351

     728 TCAACTTAGGTAGTGAAAAAATTAAACATAGCCCATATGGTTTT...... 771
         ::   ||||||:::::::::      ::::::      |||:::
     351 hrTyrLeuGlyGlyAspGluArgGlyGluGlyLysAsnGlyIleGlnLeu 367

     772 ..............TTACCAACAGGAGGCTCATTTGGCGACAGTGGCTC 806
                       |||      |||::::::::::::   ||||||
     368 AlaLysLysThrSerLeuGluLysGlySerThrIleAsnValSerGly.. 383

     807 ACCAATGTTTATCTATGATGCCCAAAAGCAAAAG.............. 840
                              |||:::|||
     384 ........................LysGluLysGlyGlyArgAlaIleV 392

     841 ..TGG............TTAATTAATGGGGTATTGCAAACG...GGCAAC 873
           |||           ||||||:::|||   :::::::::   |||:::
     392 alTrpGlyAspIleAlaLeuIleAspGlyAsnIleAsnAlaGlnGlySer 408

     874 CCCTATATAGGAAAAAGCAATGGCTTC..................... 900
               |||:::|||::::::||||||
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     901 ..............CAGCTGGTTCGT...AAAGATTGGTTCTATGATG 931
                            :::|||:::   |||:::|||:::   |||
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982 GGGAAATACTCTTTTAACGACGAT...AATAATGGCACAGGAAAAATCAA 1028
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455 AsnAsnThrGlyIleAsnAspGluPheProThrGlyThrGlyGluAlaSe 471

1029 TGCCAAACATGAACACAATTCTCTGCCTAATAGATTAAAAACACGAACCG 1078
     :          ::::::::::::|||   :::   |||   :::   |||:
471 rAspProLysLysAsnSerGluLeuLysThrThrLeuThrAsnThrThrI 488

1079 TTCAA......TTGTTTAATGTT...TCTTTATCCGAGACAGCAAGAGAA 1119
     :::::      |||   |||:::   :::|||:::   ||||||   :::
488 leSerAsnTyrLeuLysAsnAlaTrpThrLeuAsnIleThrAlaSerArg 504

1120 CCTGTTTATCATGCTGCAGGTGGTGTCAACAGTTATCGACCCAGACTGAA 1169
     :::                        |||||||||             :::||
505 LysLeu..............ThrValAsnSer.........SerIleAs 513

1170 TAATGGAGAAAATATTTCCTTTATTGACGAAGGAAAAGGCGAATTGATAC 1219
     |   |||:::|||      :::|||   ::::::||||||
513 nIleGlySerAsnSerHisLeuIleLeuHisSerLysGly..... 526

1220 TTACCAGCAACATCAATCAAGGTGCTGGAGGATTATATTTCCAAGGAGAT 1269
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527 .................GlnArgGlyGlyGlyValGlnIleAspGlyAsp 537

1270 TTTACGGTCTCGCCTGAAAATAACGAAACTTGGCAAGGCGCGGGCGTTCA 1319
     :::|||   :::      |||         ::::::|||:::   |||
538 IleThrSerLysGlyGlyAsnLeuThrIleTyrSerGlyGlyTrpValAs 554

1320 TATCAGTGAAGACAGTACCGTTACTTGGAAAGTAAACGGCGTGGCAAACG 1369
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554 pValHisLysAsnIleThrLeu..... 561

1370 ACCGCCTGTCCAAAATCGGCAAAGGCACGCTGCACGTTCAAGCCAAAGGG 1419

561 ..... 561

1420 GAAAACCAAGGCTCGATCAGCGTGGGCGACGGTACAGTCATTTTGGATCA 1469
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562 ...AspGlnGlyPheLeuAsnIleThrAlaAlaSerValAlaPhe...Gl 576

1470 GCAGGCAGACGATAAAGGCAAAAAACAAGCCTTTAGTGAAATCGGCTTGG 1519
     :   :::::::::|||::::::      |||   ::::::|||
576 uGlyGlyAsnAsnLysAlaArgAspAlaAlaAsnAlaLysIle..... 590

1520 TCAGCGGCAGGGGTACGGTGCAACTGAATGCCGATAATCAGTTCAACCCC 1569
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591 ..ValAlaGlnGlyThrValThrIleThrGlyGluGlyLys..... 603

1570 GACAAACTCTATTTCGGCTTTCGCGGCGGACGTTTGGATTTAAACGGGCA 1619
                        ||||||:::::::::::::::|||||||||
604 ..............AspPheArgAlaAsnAsnValSerLeuAsnGly.. 614

1620 TTCGCTTTCGTTCCACCGTATTCAAAATACCGATGAAGGGGCGATGATTG 1669
                                  |||   :::|||      |||:
615 ..........................ThrGlyLysGlyLeuAsnIleI 622

1670 TC............AACCACAATCAAGACAAAGAATCCACCGTTACCATT 1707
     ::            |||   :::::::::   ::::::|||:::::|||
622 leSerSerValAsnAsnLeuThrHisAsnLeuSerGlyThrIleAsnIle 638

1708 ACAGGCAATAAAGATATTGCTACAACCGGCAATAACAACAGCTTGGATAG 1757
     :::||||||      |||      |||                    ::
639 SerGlyAsnIleThrIleAsnGlnThr.....................Th 648

1758 CAAAAAAGAAATTGCCTACAACGGTTGGTTTGGCGAGAAAGATACG.... 1803
     ::::|||:::   :::|||      |||      :::   |||:::
648 rArgLysAsnThrSerTyr......TrpGlnThrSerHisAspSerHisT 663

1804 ...................ACCAAAACGAACGGGCGGCTCAACCTTGTT 1833
                         :::|||:::::::::::::::::::::::
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663 rpAsnValSerAlaLeuAsnLeuGluThrGlyAlaAsnPheThrPheIle 679

1834 TACCAGCCCGCCGCAGAAGACCGCACCCTGCTGCTT.....TC 1871
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680 LysTyrIleSerSerAsnSerLysGlyLeuThrThrGlnTyrArgSerSe 696

1872 CGGCGGAACAAATTTAAACGGCAACATCACGCAAACAAACGGCAAACTGT 1921
     |:::|||:::|||:::|||||||            :::||||||::::::
696 rAlaGlyValAsnPheAsnGly.....ValAsnGlyAsnMetS 709

1922 TTTTCAGCGGCAGACCAACACCGCACGCCTACAATCATTTA......AAC 1965
       |||:::   :::            :::         |||      |||
709 erPheAsnLeuLysGluGlyAlaLysValAsnPheLysLeuLysProAsn 725

1966 GACCATTGGTCGCAAAAAGAGGGCATTCCT..... 1995
     ::::::   :::   ::::::   :::|||
726 GluAsnMetAsnThrSerLysProLeuProIleArgPheLeuAlaAsnIl 742

1996 .............CGCGGGGAAATCGTGTGGGACAACGACTGGATCAACC 2032
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742 eThrAlaThrGlyGlyGlySerValPhePheAsp.........IleTyrA 756

2033 GCACATTTAAAGCGGAAAACTTCCAAATTAAAGGCGGACAGGCGGTGGTT 2082
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756 laAsnHisSerGlyArgGlyAlaGluLeuLysMetSerGluIleAsnIle 772

2083 TCCCGCAATGTTGCCAAAGTGAAAGGCGATTGGCATTTGAGCAATCACGC 2132
     |||:::::::                ::::::::   |||:::::::|||::
773 SerAsnGly..............AlaAsnPheThrLeuAsnSerHisVa 784

2133 CCAAGCAGTTTTTGGTGTCGCACCGCATCAAAGCCACACAATC...TGTA 2179
     ::::|||      :::         :::::::::   ||||||   :::|
784 lArgAlaAspAspAlaPheLysIleAsnLysAspLeuThrIleAsnAlaT 801

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801 hrAsnSerAsnPhe..... 805

2230 GACGATAAAGTGATTGCTTCATTGACTAAGACCGACATCAGCGGCAATGT 2279
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2280 CGATCTTGCCGATCACGCTCATTTAAATCTCACAGGGCTTGCCACACTCA 2329
           |||   :::|||      :::      :::::::::   |||:
816 pGlyTyrAlaArgAsnAlaIleAsnSerThrTyrAsnIleSerIleLeuG 833

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     ::||||||::::::   :::|||
833 lyGlyAsnValThrLeuGlyGly..... 840

2380 GCCACCCAAAACGGCAACCTTAGCCTCGTGGGCAATGCCCAAGCAACATT 2429
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841 ......GlnAsnSerSerSerSerIleThrGlyAsn......IleThrIl 853

2430 TAATCAAGCC.........ACATTAAACGGCAACACATCGGCTTCGGGCA 2470
     ::::::::|||         |||||||::::::|||::::::   :::   :
853 eGluLysAlaAlaAsnValThrLeuGluAlaAsnAsnAlaProAsnGlnG 870

2471 ATGCTTCATTTAATCTAAGCGACCACGCCGTACAAAACGGCAGTCTGACG 2520
     ::          |||:::   |||::::::::::::   |||||||||
870 ln.........AsnIleArgAspArgValIleLysLeuGlySerLeuLeu 883

2521 CTTTCCGGCAACGCTAAGGCAAACGTAAGCCATTCCGCACTCAACGGTAA 2570
     ::::::|||:::   :::   :::   :::::::::   ::::::||||
884 ValAsnGlySerLeuSerLeuThrGlyGluAsnAlaAspIleLysGlyAs 900

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     |:::::::::::::::::|||:::|||                ::::::
900 nLeuThrIleSerGluSerAlaThrPheLysGlyLysThrArgAspThrL 917

2612 GCCGCTTTACCGGACAAATCAGCGGCGGCAAGGATACGGCATTACACTTA 2661
       ::::::||||||:::::::::::::::      :::   :::::::::
917 euAsnIleThrGlyAsnPheThrAsnAsnGlyThrAlaGluIleAsnIle 933
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2712 CCTTGACAACGCCACCATTACACTCAATTCCGCCTATCGCCACGATGCGG 2761
950 nIleThrThr..... 953

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954 .....HisAlaLys 956

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957 ArgAsnGlnArgSerIleIleGlyGlyAspIleIleAsnLysLysGlySe 973

2858 AATCCCGTTTCAACACGCTGACGGTAAACGGCAAATTGAACGGTCAGGGA 2907
973 rLeuAsnIleThrAspSerAsnAsnAspAlaGluIleGlnIleGlyGlyA 990

2908 ACATTCCGCTTTATGTCGGAACTCTTCGGCTACCGCAGCGACAAATTGAA 2957
990 snIleSerGlnLysGluGlyAsnLeuThrIle.SerSerAspLysIleAs 1006

2958 GCTGGCGGAAAGTTCCGAAGGCACTTACACCTTGGCGGTCAACAATACCG 3007
1006 nIleThr..... 1008

3008 GCAACGAACCTGCAAGCCTCGAACAATTGACGGTAGTGGAAGGAAAAGAC 3057
1009 .....LysGlnIleThrIleLysLysGlyIleAsp 1018

3058 AACAAACCGCTGTCC.....GAAAACCTTAATTTCACCCTGCA 3095
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3096 AAACGAACACGTCGAT.....GCCGGCGCGTGGC 3124
1035 sThrLysGluLeuLysLeuThrGluAspLeuSerIleSerGlyPheAsnL 1052

3125 GTTACCAACTCATCCGCAAAGACGGC...GAGTTCCGCCTGCATAATCCG 3171
1052 ysAlaGluIleThrAlaLysAspGlyArgAspLeuThrIleGlyAsnSer 1068

3172 GTCAAAGAACAAGAGCTTTCCGACAAACTCGGCAAGGCAGAAGCCAAAAA 3221
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3272 GGCGCGATGCCGTCGAAAAGACAGAAAGCGTTGCCGAACCGGCCCGGCAG 3321
1093 spGlyHisAsnValThrLeuAsnSerLysValLysThrSerSerSerAsn 1109

3322 GCAGGCGGGGAAAATGTCGGCATTATGCAGGCGGAGGAAGAGAAAAAACG 3371
1110 GlyGlyArgGluSer..... 1114

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1135 IleThrSerLeu..... 1138

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3672 GC...AAGATTTCCGCGCCTACCGCCAACAAACCGACCTGCGCCAAATCG 3718
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3719 GTATGCAGAAAAACCTCGGCAGCGGGCGCGTCGGCATCCTGTTTTCGCAC 3768
1204 GluAlaAsnValThrSerAlaThrGlyThrIleGlyGly.....Th 1217

3769 AACCGGACCGAAAACACCTTCGACGACGGCATCGGCA..... 3805
1217 rIleSerGlyAsnThrValAsnValThrAlaAsnAlaGlyAspLeuThrV 1234

3806 .....ACTCGGCACGGCTTGCCCACGGCGCCG 3832
1234 alGlyAsnGlyAlaGluIleAsnAlaThrGluGlyAlaAlaThrLeuThr 1250

3833 TTTTCGGGCAATACGGCATCGACA......GGTTCTACATCGGCATCAGC 3876
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3877 GCGGGCGCGGGTTTTAGCAGCGGCAGCCTTTCAGACGGCATCGGAGGCAA 3926
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3927 AATCCGCCGCCGCGTGCTGCATTACGGCATTCAGGCACGATACCGCGCCG 3976
1282 lySerIleAsnAlaAlaAsnValThrLeuAsnThrThrGlyThrLeuThr 1298

3977 GTTTCGGCGGATTCGGCATCGAACCGCACATCGGCGCAACGCGCTATTTC 4026
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4027 GTCCAAA 4033
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seq_documentation_block:

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AC   AAR41724;
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DT   26-APR-1994  (first entry)
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DE   High molecular weight protein 2 (HMW2).
XX
KW   HMW; high molecular weight protein; virus; vaccine; influenza;
KW   epitope; immunity; haemophilus influenzae.
XX
OS   Haemophilus influenzae.
XX
PN   WO9319090-A.
XX
PD   30-SEP-1993.
XX
PF   16-MAR-1993;   93WO-US02166.
XX
PR   16-MAR-1992;   92GB-0005704.
XX
PA   (BARE/) BARENKAMP S J.
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PA (INRM) INSERM INST NAT SANTE & RECH MEDICALE.
XX
PI Barenkamp SJ;
XX
DR WPI; 1993-320683/40.
DR N-PSDB; AAQ49507.
XX
PT High molecular weight surface proteins - of non-typeable
PT haemophilus which exhibit immunogenic properties
XX
PS Claim 4; Figure 4; 100pp; English.
XX
CC The isolation and purification of the high molecular weight protein
CC enables the identification of the major protective epitopes of the
CC protein by conventional epitope mapping. These epitopes can then be
CC synthesised using standard techniques and incorporated into fully
CC synthetic or recombinant vaccines.
XX
SQ Sequence 1477 AA;

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Ratio: 0.432 Gaps: 61
Percent Similarity: 47.622 Percent Identity: 19.380

alignment_block:
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Align seg 1/1 to: AAR41724 from: 1 to: 1477

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175 GAAAATAAAGGCAAGTTTGCAGTCGGGGCGAAAGATATTGAGGTTTACAA 224
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219 LysAsnGluGlyValIleSerValAsnGlyGlySerIleSerLeu..... 233

225 CAAAAAAGGGGAGTTGGTCGGCAAATCAATGACAAAAGCC.......... 264
                |||:::|||:::::::::|||   :::
234 .............LeuAlaGlyGlnLysIleThrIleSerAspIleIleA 246

265 ..CCGATGATTGATTTTTCTGTGGTGTCGCGTAACGGCGTGGCGGCATTG 312
      |||   |||   :::|||:::::::::   ::::::   |||:::
246 snProThrIleThrTyrSerIleAlaAlaProGluAsnGluAlaValAsn 262

313 GTGGGCGATCAATATATTGTGAGCGTGGCACATAACGGCGGCTATAACAA 362
    :::||||||              :::      :::||||||      ||
263 LeuGlyAsp..............IlePheAlaLysGlyGlyAsnIleAs 274

363 CGTT..........................GATTTTGGTGCGGAAGGAA 385
    ||||                        :::::::|||::::::
274 nValArgAlaAlaThrIleArgAsnGlnGlyLysLeuSerAlaAspServ 291

386 GAAATCCCGATCAACATCGTTTTACTTATAAAATTGTGAAACGGAATAAT 435
      :::   |||:::                    :::|||::::::::
291 alSerLysAspLysSerGlyAsnIleValLeuSerAlaLysGluGlyGlu 307

436 TATAAAGCAGGG..............ACTAAAGGCCATCCTTATGGCGG 470
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308 AlaGluIleGlyGlyValIleSerAlaGlnAsnGlnGlnAlaLysGlyGl 324

471 CGATTATCATATGCCGCGTTTGCATAAATTTGTCACAGATGCAGAACCTG 520
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324 yLysLeuMetIleThrGlyAspLysValThrLeuLysThrGlyAlaValI 341

521 TTGAAATGACCAGTTATATGGATGGGCGGAAATATATCGATCAAAATAAT 570
    :::::::::::::        |||:::   |||:::      :::::::
341 leAspLeuSerGlyLysGluGlyGlyGluThrTyrLeuGlyGlyAspGlu 357

571 TACCCTGACCGTGTTCGTATTGGGGCAGGCAGGCAATATTGGCGATCTGA 620
                      |||   |||::::::      :::
358 Arg.................GlyGluGlyLysAsnGlyIleGlnLeuAl 368

621 TGAAGATGAGCCCAATAACCGCGAAAGTTCATATCATATTGCAAGT.... 666
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368 aLysLysThrSerLeuGluLysGlySerThrIleAsnValSerGlyLysG 385

667 .............GCGTATTCTTGG............CTCGTTGGTGGC 690
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385 luLysGlyGlyArgAlaIleValTrpGlyAspIleAlaLeuIleAspGly 401

691 AATACCTTTGCACAAAATGGATCAGGTGGTGGCACAGTCAACTTAGGTAG 740
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402 AsnIleAsnAlaGln...GlySerGly..................... 409

741 TGAAAAAATTAAACATAGCCCATATGGTTTTTTACCAACAGGAGGCTCAT 790
                                    :::      |||||||||
410 .........................AspIleAlaLysThrGlyGlyPheV 418

791 TTGGCGACAGTGGCTCACCAATGTTTATCTATGATGCCCAAAAGCAAAAG 840
          ||||||      :::||||||   |||
418 alGluThrSerGlyHisAspLeuPheIleLysAsp.............. 429

841 TGGTTAATTAATGGGGTATTGCAAACGGGCAACCCCTATATAGGAAAAAG 890
          |||:::::::::::::::
430 .........AsnAlaIleValAspAla...................... 435

891 CAATGGCTTCCAGCTGGTTCGTAAAGATTGGTTCTATGATGAAATCTTTG 940
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436 .....................LysGluTrpLeuLeuAsp.......... 441

941 CTGGAGATACCCATTCAGTATTCTACGAACCACGTCAAAATGGGAAATAC 990
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991 TCTTTTAACGACGAT...AATAATGGCACAGGAAAAATCAATGCCAAACA 1037
    ::::::||||||:::      :::|||||||||:::   :::
458 GlyIleAsnAspGluPheProThrGlyThrGlyGluAlaSerAspProLy 474

1038 TGAACACAATTCTCTGCCTAATAGATTAAAAACACGAACCGTTCAATTGT 1087
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474 sLysAsnSerGluLeuLysThrThrLeuThrAsnThrThrIleSerAsnT 491

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     ::                     |||::::::   |||:::
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508 ..........................ValAsnSer.........SerIl 512

1167 GAATAATGGAGAAAATATTTCCTTTATTGACGAAGGAAAAGGCGAATTGA 1216
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1217 TACTTACCAGCAACATCAATCAAGGTGCTGGAGGATTATATTTCCAAGGA 1266
                                |||   :::|||||||:::   ::::::|||
527 ...................GlnArgGlyGlyGlyValGlnIleAspGly 536

1267 GATTTTACGGTCTCGCCTGAAAATAACGAAACTTGGCAAGGCGCGGGCGT 1316
     |||:::|||   :::      |||         ::::::|||:::   ||
537 AspIleThrSerLysGlyGlyAsnLeuThrIleTyrSerGlyGlyTrpVa 553

1317 TCATATCAGTGAAGACAGTACCGTTACTTGGAAAGTAAACGGCGTGGCAA 1366
     |   :::   ::::::   |||:::
553 lAspValHisLysAsnIleThrLeu..................... 561

1367 ACGACCGCCTGTCCAAAATCGGCAAAGGCACGCTGCACGTTCAAGCCAAA 1416

561 ..................................................... 561

1417 GGGGAAAACCAAGGCTCGATCAGCGTGGGCGACGGTACAGTCATTTTGGA 1466
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562 ......AspGlnGlyPheLeuAsnIleThrAlaAlaSerValAlaPhe.. 575

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576 .GluGlyGlyAsnAsnLysAlaArgAspAlaAlaAsnAlaLysIle.... 590
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591 .....ValAlaGlnGlyThrValThrIleThrGlyGluGlyLys.....,  603

1567 CCCGACAAACTCTATTTCGGCTTTCGCGGCGGACGTTTGGATTTAAACGG 1616
604 .................AspPheArgAlaAsnAsnValSerLeuAsnGl  614

1617 GCATTCGCTTTCGTTCCACCGTATTCAAAATACCGATGAAGGGGCGATGA 1666
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1667 TTGTC............AACCACAATCAAGACAAAGAATCCACCGTTACC 1704
621 leIleSerSerValAsnAsnLeuThrHisAsnLeuSerGlyThrIleAsn  637

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638 IleSerGlyAsnIleThrIleAsnGlnThr.....  647

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1804 .....ACCAAAACGAACGGGCGGCTCAACCTT 1830
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695 rSerAlaGlyValAsnPheAsnGly............ValAsnGlyAsnM  708

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708 etSerPhe.....  710

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711 ......AsnLeuLysGluGlyAlaLysValAsnPheLysLeuLysProAs  725

2019 CGACTGGATCAACCGCACA.................TTTAAAGCGGAAA 2050
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2051 ACTTCCAAATTAAAGGCGGACAGGCGGTGGTT..... 2082
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2127 TCACGCCCAAGCAGTTTTTGGTGTCGCACCGCATCAAAGCCACACAATCT 2176
774 nGlyAlaAsnPheThrLeu..............AsnSerHis.......  783

2177 GTACACGTTCGGACTGGACGGGTCTGACAAATTGTGTCGAAAAAACCATT 2226
784 ..ValArgGlyAspAspAlaPheLysIleAsn...LysAspLeuThrIle  798

2227 ACCGACGATAAAGTGATTGCTTCATTGACTAAGACCGACATCAGCGGCAA 2276
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2568 TAATGTCTCCCTAGCCGATAAGGCAGTATTCCAT.........TTTGAAA 2608
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2609 GCAGCCGCTTTACCGGACAAATCAGCGGCGGCAAGGATACGGCATTACAC 2658
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2709 AAACCTTGACAACGCCACCATTACACTCAATTCCGCCTATCGCCACGATG 2758
949 uAsnIleThrThr.....  953

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2855 TAGAATCCCGTTTCAACACGCTGACGGTAAACGGCAAATTGAACGGTCAG 2904
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3093 GCAAAACGAACACGTCGAT.....................GCCGGCGCGT 3121
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1092 laAspGlyHisAsnValThrLeuAsnSerLysValLysThrSerSerSer 1108

3319 CAGGCAGGCGGGGAAAATGTCGGCATTATGCAGGCGGAGGAAGAGAAAAA 3368
     :::::::|||   |||:::
1109 AsnGlyGlyArgGluSer.............................. 1114

3369 ACGGGTGCAGGCGGATAAAGACACCGCCTTGGCGAAACAGCGCGAAGCGG 3418
           ::::::|||:::||||||:::|||
1115 .......AsnSerAspAsnAspThrGlyLeu..................... 1122

3419 AAACCCGGCCGGCTACCACCGCCTTCCCCCGCGCCCGCCGCGCCCGCCGG 3468
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1123 .................ThrIleThrAlaLysAsnValGluValAsnLys 1133

3469 GATTTGCCGCAACTGCAACCCCAACCGCAGCCCCAACCGCAGCGCGACCT 3518
     |||:::   :::|||
1134 AspIleThrSerLeu................................... 1138

3519 GATCAGCCGTTATGCCAATAGCGGTTTGAGTGAATTTTCCGCCACGCTCA 3568
           :::   :::|||        ||||||      :::||| :::
1139 .......LysThrValAsnIleThrAlaSerGluLysValThrThr.Thr 1152

3569 ACAGCGTTTTCGCCGTACAGGACGAATTAGACCGCGTATTTGCCGAAGAC 3618
     ::::::   :::         ||||||      |||   :::
1153 AlaGlySerThrIleAsnAlaThrAsnGlyLysAlaSerIleThrThrLy 1169

3619 CGCCGCAACGCCGTTTGGACAAGCGGCATCCGGGACACCAAACACTACCG 3668
      ::::::         |||      ::::::::::|||   ::::::::::
1169 sThrGlyAspIleSerGlyThrIleSerGlyAsnThrValSerValSerA 1186

3669 TTCGC...AAGATTTCCGCGCCTACCGCCAACAAACCGACCTGCGCCAAA 3715
     ::         :::::::::   :::::::::|||      :::   :::
1186 laThrValAspLeuThrThrLysSerGlySerLysIleGluAlaLysSer 1202

3716 TCGGTATGCAGAAAAACCTCGGCAGCGGGCGCGTCGGCATCCTGTTTTCG 3765
     :::   ::::::   |||||||||:::|||:::   ::::::
1203 GlyGluAlaAsnValThrSerAlaThrGlyThrIleGlyGly........ 1216

3766 CACAACCGGACCGAAAACACCTTCGACGACGGCATCGGCA.......... 3805
      |||   :::   :::|||   ::::::||||||:::|||
1217 .ThrIleSerGlyAsnThrValAsnValThrAlaAsnAlaGlyAspLeuT 1233

3806 .........................ACTCGGCACGGCTTGCCCACGGCG 3829
                               :::   :::|||      |||
1233 hrValGlyAsnGlyAlaGluIleAsnAlaThrGluGlyAlaAlaThrLeu 1249

3830 CCGTTTTCGGGCAATACGGCATCGACA......GGTTCTACATCGGCATC 3873
          :::|||||||||   :::|||      ||||||:::   :::||
1250 ThrAlaThrGlyAsnThrLeuThrThrGluAlaGlySerSerIleThrSe 1266

3874 AGCGCGGGCGCGGGTTTTAGCAGCGGCAGCCTTTCAGACGGCATCGGAGG 3923
     |:::::::::::|||         |||      |||:::::::|||   |
1266 rThrLysGlyGlnValAspLeuLeuAla......GlnAsnGlySerIleA 1281

3924 CAAAATCCGCCGCCGCGTGCTGCATTACGGCATTCAGGCACGATACCGCG 3973
     ||   |||      |||:::   :::|||                |||
1281 laGlySerIleAsnAlaAlaAsnValThrLeuAsnThrThrGlyThrLeu 1297

3974 CCGGTTTCGGCGGATTCGGCATCGAACCGCACATCGGCGCAACGCGCTAT 4023
        :::   |||   |||      :::   ||||||:::      :::||
1298 ThrThrValAlaGlySerAspIleLysAlaThrSerGlyThrLeuValIl 1314

4024 TTCGTCCAAA 4033
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1314 eAsnAlaLys 1317

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seq_documentation_block:
ID   AAR41728 standard; Protein; 1477 AA.
XX
AC   AAR41728;
XX
DT   26-APR-1994  (first entry)
XX
DE   High molecular weight protein 2 (HMW2).
XX
KW   HMW; high molecular weight protein; virus; vaccine; influenza;
KW   epitope; immunity; haemophilus influenzae; gene cluster.
XX
OS   Haemophilus influenzae.
XX
PN   WO9319090-A.
XX
PD   30-SEP-1993.
XX
PF   16-MAR-1993;   93WO-US02166.
XX
PR   16-MAR-1992;   92GB-0005704.
XX
PA   (BARE/) BARENKAMP S J.
PA   (INRM ) INSERM INST NAT SANTE & RECH MEDICALE.
XX
PI   Barenkamp SJ;
XX
DR   WPI; 1993-320683/40.
DR   N-PSDB; AAQ49509.
XX
PT   High molecular weight surface proteins - of non-typeable
PT   haemophilus which exhibit immunogenic properties
XX
PS   Claim 4; Figure 4; 100pp; English.
XX
CC   The isolation and purification of the high molecular weight protein
CC   enables the identification of the major protective epitopes of the
CC   protein by conventional epitope mapping.  These epitopes can then be
CC   synthesised using standard techniques and incorporated into fully
CC   synthetic or recombinant vaccines.  This sequence is claimed to be
CC   the same as that given in AAR41724 (High molecular weight protein 2)
CC   although it does differ slightly.
XX
SQ   Sequence   1477 AA;


alignment_scores:
            Quality:  285.00              Length:   1441
              Ratio:  0.417                 Gaps:     67
 Percent Similarity:  47.398   Percent Identity: 19.778

alignment_block:
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     158 LysAspAlaIleIleAsnThrAsnGlyPheThrAlaSerThrLeuAspIl 174

     213 TGAGGTTTACAACAAAAAAGGGGAGTTGGTCGGCAAATCAATGACAAAA. 261
         |:::      |||   |||:::::::             ::::::||||||
     174 eSerAsnGluAsnIleLysAlaArgAsnPheThrPheGluGlnThrLysA 191

     262 ..........GCCCCGATGATTGATTTTTCTGTG......GTGTCGCGT 294
                    |||   :::::::::   ::::::      |||::::::
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     295 AACGGCGTGGCGGCATTGGTGGGC...........GATCAATATATTGT 332
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208 AspGlySerValAsnLeuIleGlyGlyLysValLysAsnGluGlyValIl 224

333 GAGCGTGGCACATAACGGCGGCTATAACAACGTTGATTTTGGT..... 375
224 eSerVal......AsnGlyGlySerIleSerLeuLeuAlaGlyGlnLysI 239

376 ........GCGGAAGGAAGAAATCCCGATCAACATCGTTTTACTTATAAA 417
239 leThrIleSerAspIleIleAsnPro.........ThrIleThrTyrSer 252

418 ATTGTGAAACGGAATAATTATAAAGCAGGGACTAAAGGCCATCCTTAT.. 465
253 IleAlaAlaProGluAsn...GluAlaValAsnLeuGlyAspIlePheAl 268

466 ....GGCGGCGATTATCATATGCCGCGTTTGCATAAATTTGTCACAGATG 511
268 aLysGlyGlyAsnIleAsn.............................. 274

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274 .............................................. 274

562 CAAAATAATTACCCTGACCGTGTTCGTATTGGGGCAGGCAGGCAATATTG 611
275 .....................ValArgAlaAlaThrIleArgAsnGlnGl 284

612 GCGATCTGATGAAGATGAGCCCAATAACCGCGAAAGTTCATATCATATTG 661
284 yLysLeuSerAlaAspSerValSerLysAspLysSerGlyAsnIleValL 301

662 CAAGTGCGTATTCTTGG......CTCGTTGGTGGCAATACCTTTGCACAA 705
301 euSerAlaLysGluGlyGluAlaGluIleGlyGlyValIleSerAlaGln 317

706 AAT............................................. 708
318 AsnGlnGlnAlaLysGlyGlyLysLeuMetIleThrGlyAspLysValTh 334

709 ..............................GGATCAGGTGGTGGCACAG 727
334 rLeuLysThrGlyAlaValIleAspLeuSerGlyLysGluGlyGlyGluT 351

728 TCAACTTAGGTAGTGAAAAAATTAAACATAGCCCATATGGTTTT..... 771
351 hrTyrLeuGlyGlyAspGluArgGlyGluGlyLysAsnGlyIleGlnLeu 367

772 ..............TTACCAACAGGAGGCTCATTTGGCGACAGTGGCTC 806
368 AlaLysLysThrSerLeuGluLysGlySerThrIleAsnValSerGly.. 383

807 ACCAATGTTTATCTATGATGCCCAAAAGCAAAAG.............. 840
384 ........................LysGluLysGlyGlyArgAlaIleV 392

841 ..TGG............TTAATTAATGGGGTATTGCAAACG...GGCAAC 873
392 alTrpGlyAspIleAlaLeuIleAspGlyAsnIleAsnAlaGlnGlySer 408

874 CCCTATATAGGAAAAAGCAATGGCTTC..................... 900
409 GlyAspIleAlaLysThrGlyGlyPheValGluThrSerGlyHisTyrLe 425

901 ..............CAGCTGGTTCGT...AAAGATTGGTTCTATGATG 931
425 uSerIleAspSerAsnAlaIleValLysThrLysGluTrpLeuLeuAspP 442

932 AAATCTTTGCTGGAGATACCCATTCAGTATTCTACGAACCACGTCAAAAT 981
442 ro............AspAspValThrIleGluAlaGluAspProLeuArg 454

982 GGGAAATACTCTTTTAACGACGAT...AATAATGGCACAGGAAAAATCAA 1028

455 AsnAsnThrGlyIleAsnAspGluPheProThrGlyThrGlyGluAlaSe 471

1029 TGCCAAACATGAACACAATTCTCTGCCTAATAGATTAAAAACACGAACCG 1078
471 rAspProLysLysAsnSerGluLeuLysThrThrLeuThrAsnThrThrI 488

1079 TTCAATTGTTT.....................AATGTTTCTTTATCCGAG 1107
488 leSerAsnTyrLeuLysAsnAlaTrpThrMetAsnIleThrAlaSerArg 504

1108 ACAGCAAGAGAACCTGTTTATCATGCTGCAGGTGGTGTCAACAGTTATCG 1157
505 LysLeuThr.........................ValAsnSer..... 510

1158 ACCCAGACTGAATAATGGAGAAAATATTTCCTTTATTGACGAAGGAAAAG 1207
511 ....SerIleAsnIleGlySerAsnSerHisLeuIleLeuHisSerLysG 526

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550 yGlyTrpValAspValHisLysAsnIleThrLeu.............. 561

1358 GCGTGGCAAACGACCGCCTGTCCAAAATCGGCAAAGGCACGCTGCACGTT 1407

561 .............................................. 561

1408 CAAGCCAAAGGGGAAAACCAAGGCTCGATCAGCGTGGGCGACGGTACAGT 1457
562 ..............AspGlnGlyPheLeuAsnIleThrAlaAlaSerVa 573

1458 CATTTTGGATCAGCAGGCAGACGATAAAGGCAAAAAACAAGCCTTTAGTG 1507
573 lAlaPhe...GluGlyGlyAsnAsnLysAlaArgAspAlaAlaAsnAlaL 589

1508 AAATCGGCTTGGTCAGCGGCAGGGGTACGGTGCAACTGAATGCCGATAAT 1557
589 ysIle.........ValAlaGlnGlyThrValThrIleThrGlyGluGly 602

1558 CAGTTCAACCCCGACAAACTCTATTTCGGCTTTCGCGGCGGACGTTTGGA 1607
603 Lys.......................AspPheArgAlaAsnAsnValSe 611

1608 TTTAAACGGGCATTCGCTTTCGTTCCACCGTATTCAAAATACCGATGAAG 1657
611 rLeuAsnGly............................ThrGlyLysG 618

1658 GGGCGATGATTGTC............AACCACAATCAAGACAAAGAATCC 1695
618 lyLeuAsnIleIleSerSerValAsnAsnLeuThrHisAsnLeuSerGly 634

1696 ACCGTTACCATTACAGGCAATAAAGATATTGCTACAACCGGCAATAACAA 1745
635 ThrIleAsnIleSerGlyAsnIleThrIleAsnGlnThr........... 647

1746 CAGCTTGGATAGCAAAAAAGAAATTGCCTACAACGGTTGGTTTGGCGAGA 1795
648 ..........ThrArgLysAsnThrSerTyr......TrpGlnThrSerH 659

1796 AAGATACG.......................ACCAAAACGAACGGGCGG 1821
659 isAspSerHisTrpAsnValSerAlaLeuAsnLeuGluThrGlyAlaAsn 675

1822 CTCAACCTTGTTTACCAGCCCGCCGCAGAAGACCGCACCCTGCTGCTT.. 1869
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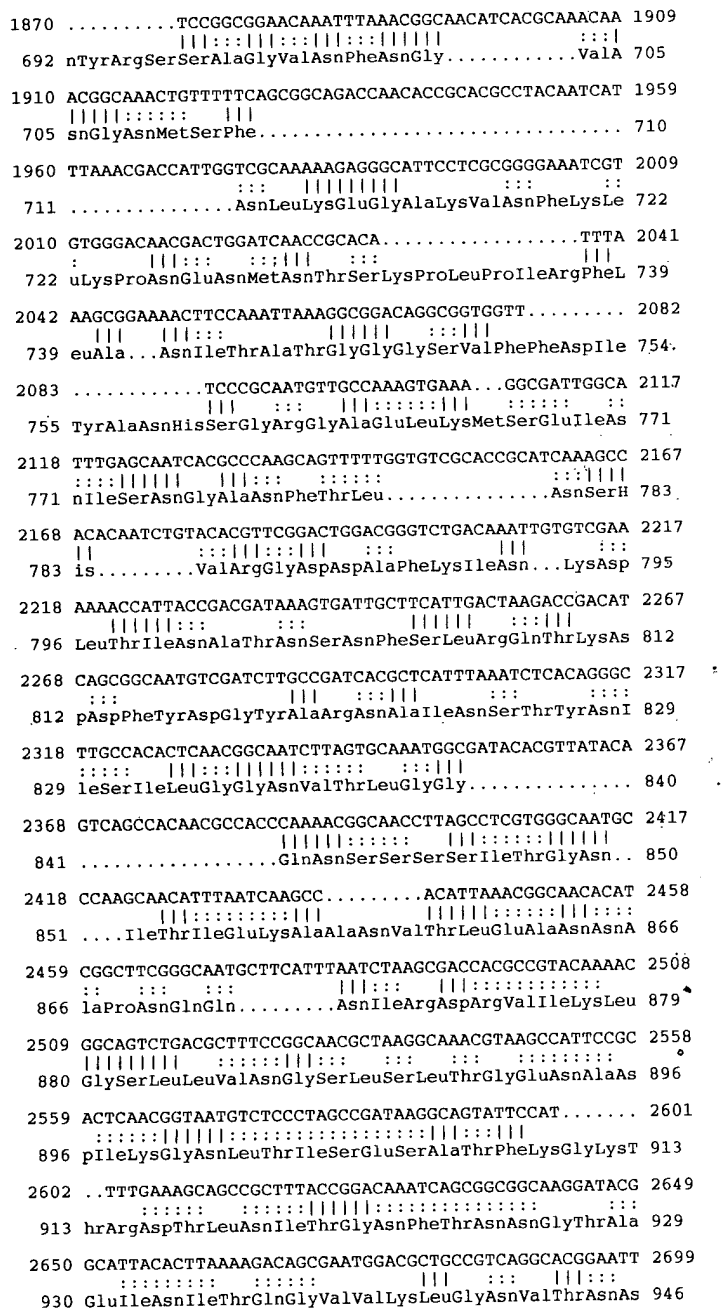

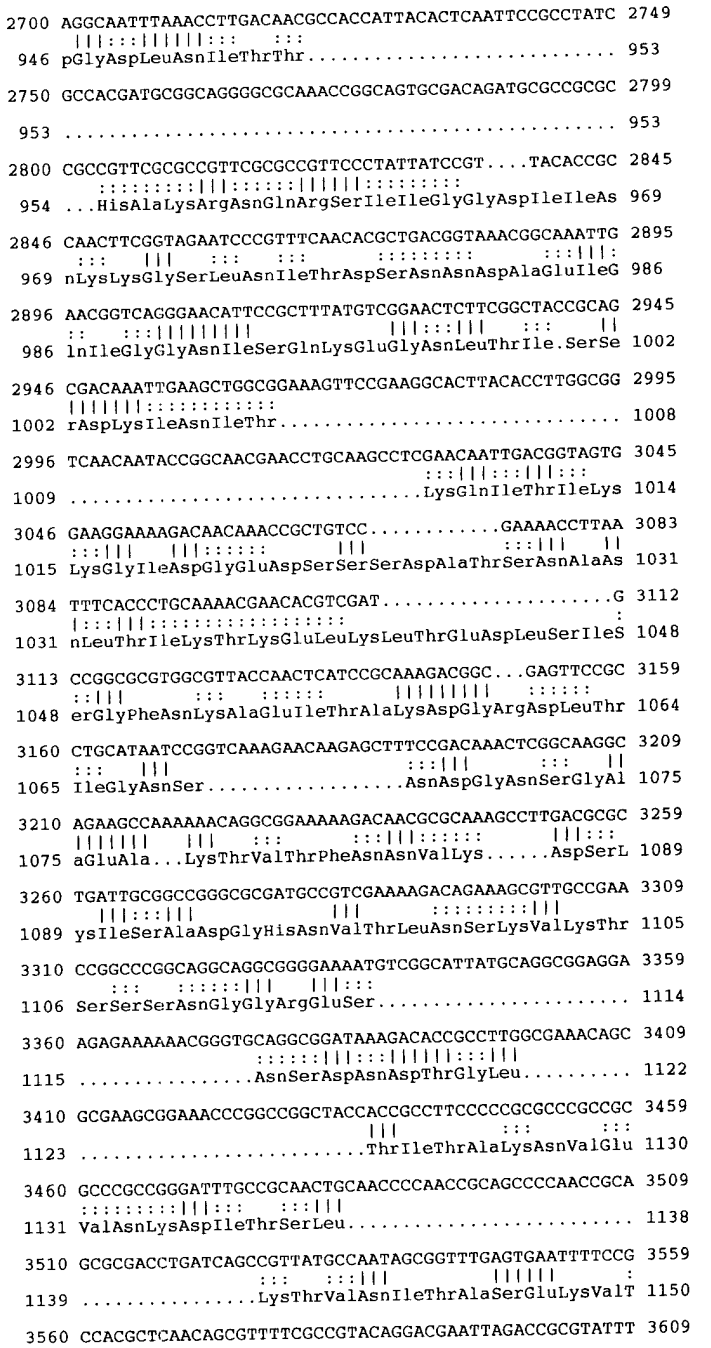

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  1166 eThrThrLysThrGlyAspIleSerGlyThrIleSerGlyAsnThrValS 1183

  3660 ACACTACCGTTCGC...AAGATTTCCGCGCCTACCGCCAACAAACCGACC 3706
       ::::::::::         :::::::::   :::::::::|||
  1183 erValSerAlaThrGlyAspLeuThrThrLysSerGlySerLysIleGlu 1199

  3707 TGCGCCAAATCGGTATGCAGAAAAACCTCGGCAGCGGGCGCGTCGGCATC 3756
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  1200 AlaLysSerGlyGluAlaAsnValThrSerAlaThrGlyThrIleGlyGl 1216

  3757 CTGTTTTCGCACAACCGGACCGAAAACACCTTCGACGACGGCATCGGCA. 3805
       :          |||   :::   :::|||   ::::::||||||:::|||
  1216 y.........ThrIleSerGlyAsnThrValAsnValThrAlaAsnAlaG 1230

  3806 ................................ACTCGGCACGGCTTG 3820
                                        :::   :::|||
  1230 lyAspLeuThrValGlyAsnGlyAlaGluIleAsnAlaThrGluGlyAla 1246

  3821 CCCACGGCGCCGTTTTCGGGCAATACGGCATCGACA......GGTTCTAC 3864
         |||         :::||||||||||   :::|||      ||||||::
  1247 AlaThrLeuThrAlaThrGlyAsnThrLeuThrThrGluAlaGlySerSe 1263

  3865 ATCGGCATCAGCGCGGGCGCGGGTTTTAGCAGCGGCAGCCTTTCAGACGG 3914
       :   :::|||:::::::::::::|||         |||      |||::::
  1263 rIleThrSerThrLysGlyGlnValAspLeuLeuAla......GlnAsnG 1278

  3915 CATCGGAGGCAAAATCCGCCGCCGCGTGCTGCATTACGGCATTCAGGCAC 3964
       ::|||   |||   |||       |||:::   :::|||
  1278 lySerIleAlaGlySerIleAsnAlaAlaAsnValThrLeuAsnThrThr 1294

  3965 GATACCGCGCCGGTTTCGGCGGATTCGGCATCGAACCGCACATCGGCGCA 4014
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  1295 GlyThrLeuThrThrValAlaGlySerAspIleLysAlaThrSerGlyTh 1311

  4015 ACGCGCTATTTCGTCCAAA 4033
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  1311 rLeuValIleAsnAlaLys 1317
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seq_documentation_block:

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ID   AAB01848 standard; Protein; 1477 AA.
XX
AC   AAB01848;
XX
DT   11-SEP-2000  (first entry)
XX
DE   Haemophilus influenzae strain 12 HMW2A protein, SEQ ID NO:71.
XX
KW   HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW   non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW   recombinant production; Escherichia coli; antibacterial; vaccine;
KW   human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW   detection; diagnosis.
XX
OS   Haemophilus influenzae strain 12.
XX
PN   WO200020609-A2.
XX
PD   13-APR-2000.
XX
PF   07-OCT-1999;   99WO-CA00938.
XX
PR   07-OCT-1998;   98US-0167568.
PR   08-DEC-1998;   98US-0206942.
XX
PA   (CONN-) CONNAUGHT LAB LTD.
XX
PI   Loosmore SM,  Yang Y,  Klein MH;
XX
DR   WPI; 2000-303789/26.
DR   N-PSDB; AAA52197.
XX
PT   Nucleic acid molecule for producing recombinant high molecular weight
PT   proteins of Haemophilus which are used as a vaccine to provide
PT   protection against Haemophilus induced diseases in humans -
XX
PS   Example 16; Fig 29A-N; 307pp; English.
XX
CC   The invention relates to the recombinant production of Haemophilus
CC   influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC   expression construct used to effect recombinant expression comprises a
CC   promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC   to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC   influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC   clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC   hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC   and the hmwB and hmwC genes encode accessory proteins which are
CC   responsible for post-translational processing and secretion of the HMWA
CC   proteins. The modified hmwABC operon used in the expression construct of
CC   the invention contains an A gene modified such that it encodes only the
CC   mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC   and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC   strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC   vectors are used for the production of recombinant H. influenzae HMW
CC   proteins which can be used as vaccines to mediate a humoral or
CC   cell-mediated immune response to provide protection against diseases in
CC   humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC   pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC   antigens in immunoassays for detecting antibodies against Haemophilus,
CC   HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC   HMW proteins can be used to isolate and clone hmw genes from other
CC   non-typeable strains of Haemophilus via hybridisation reactions. The
CC   present sequence represents an HMWA protein from a non-typeable strain of
CC   H. influenzae.
XX
SQ   Sequence   1477 AA;
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alignment_scores:

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            Quality:  285.00              Length:   1441
              Ratio:  0.417                 Gaps:     67
 Percent Similarity:  47.398   Percent Identity: 19.778
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alignment_block:

US-09-303-518D-649 x AAB01848 ..

Align seg 1/1 to: AAB01848 from: 1 to: 1477

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    158 LysAspAlaIleIleAsnThrAsnGlyPheThrAlaSerThrLeuAspIl 174

    213 TGAGGTTTACAACAAAAAAGGGGAGTTGGTCGGCAAATCAATGACAAAA. 261
        |:::      |||   |||::::::            :::::::||||||
    174 eSerAsnGluAsnIleLysAlaArgAsnPheThrPheGluGlnThrLysA 191

    262 ...........GCCCCGATGATTGATTTTTCTGTG......GTGTCGCGT 294
                   |||   :::::::::   ::::::      |||::::::
    191 spLysAlaLeuAlaGluIleValAsnHisGlyLeuIleThrValGlyLys 207

    295 AACGGCGTGGCGGCATTGGTGGGC............GATCAATATATTGT 332
        :::|||   :::   |||:::|||            ::::::   :::::
    208 AspGlySerValAsnLeuIleGlyGlyLysValLysAsnGluGlyValIl 224

    333 GAGCGTGGCACATAACGGCGGCTATAACAACGTTGATTTTGGT..... 375
        :||||||      |||||||||      ::::::      |||
    224 eSerVal......AsnGlyGlySerIleSerLeuLeuAlaGlyGlnLysI 239

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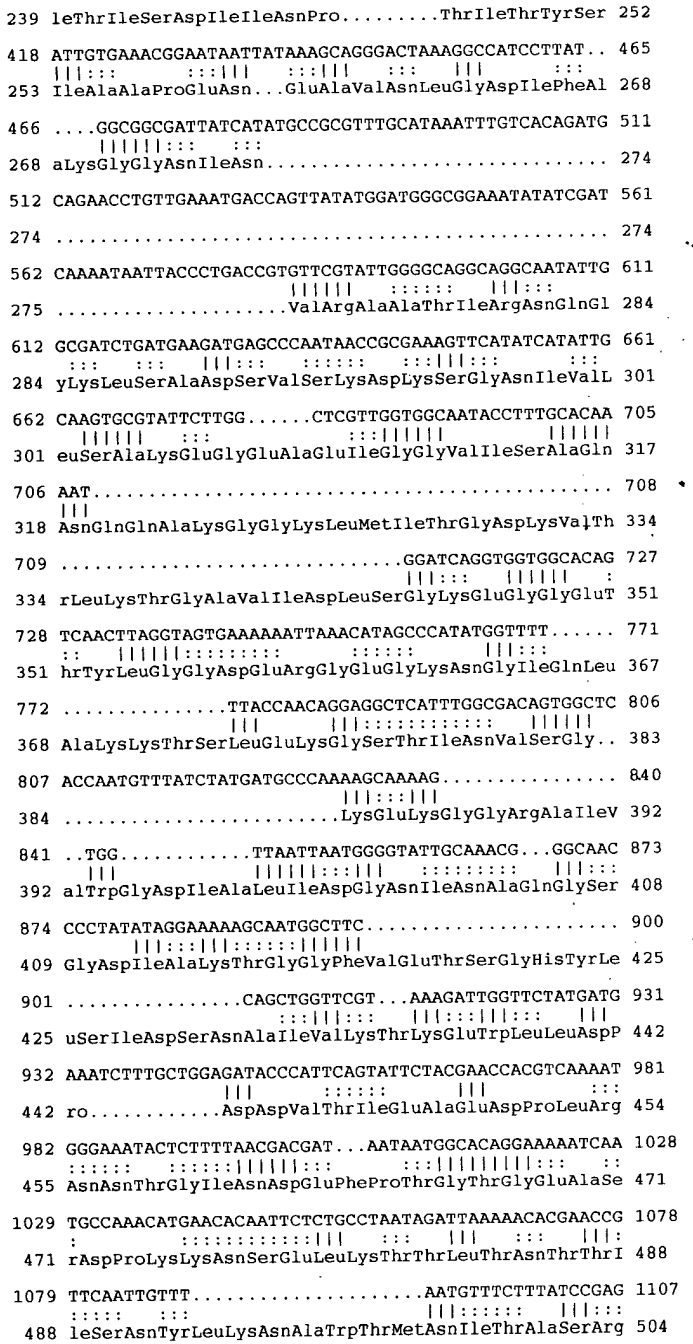

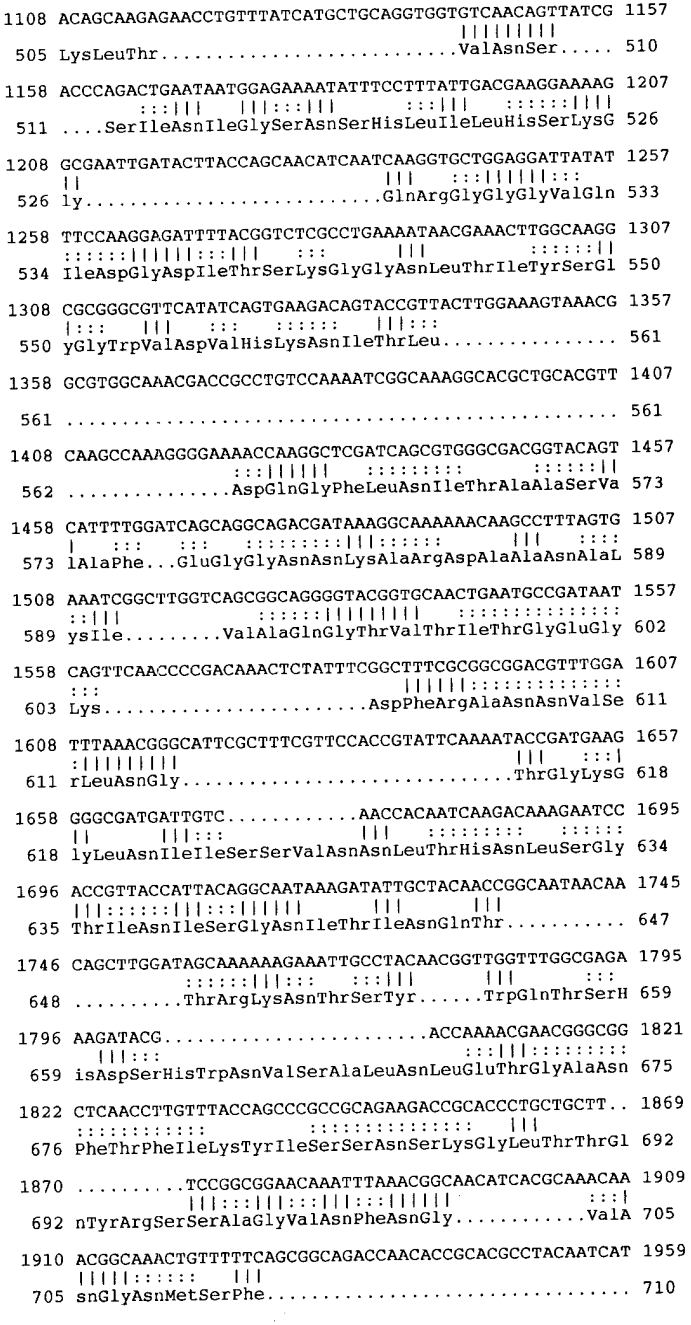

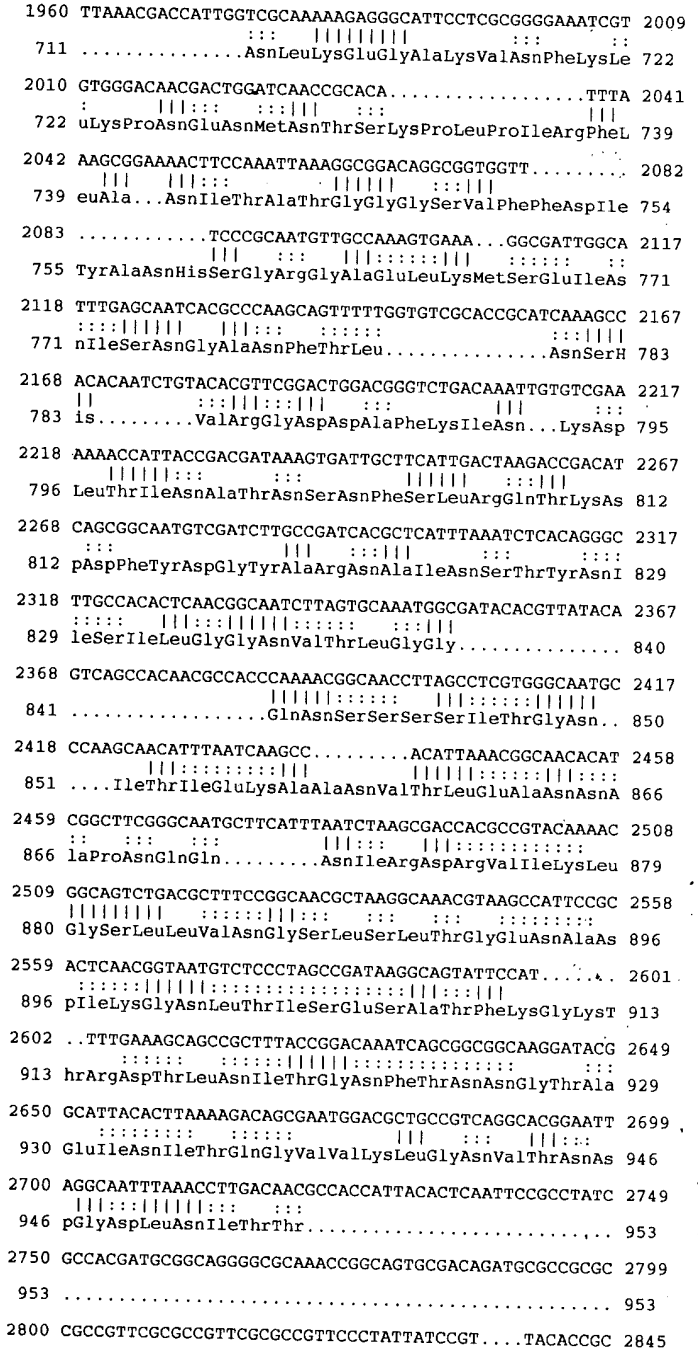
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2042 AAGCGGAAAACTTCCAAATTAAAGGCGGACAGGCGGTGGTT..... 2082
739 euAla...AsnIleThrAlaThrGlyGlySerValPhePheAspIle 754
2083 .....TCCCGCAATGTTGCCAAAGTGAAA...GGCGATTGGCA 2117
755 TyrAlaAsnHisSerGlyArgGlyAlaGluLeuLysMetSerGluIleAs 771
2118 TTTGAGCAATCACGCCCAAGCAGTTTTTGGTGTCGCACCGCATCAAAGCC 2167
771 nIleSerAsnGlyAlaAsnPheThrLeu.....AsnSerH 783
2168 ACACAATCTGTACACGTTCGGACTGGACGGGTCTGACAAATTGTGTCGAA 2217
783 is.....ValArgGlyAspAspAlaPheLysIleAsn...LysAsp 795
2218 AAAACCATTACCGACGATAAAGTGATTGCTTCATTGACTAAGACCGACAT 2267
796 LeuThrIleAsnAlaThrAsnSerAsnPheSerLeuArgGlnThrLysAs 812
2268 CAGCGGCAATGTCGATCTTGCCGATCACGCTCATTTAAATCTCACAGGGC 2317
812 pAspPheTyrAspGlyTyrAlaArgAsnAlaIleAsnSerThrTyrAsnI 829
2318 TTGCCACACTCAACGGCAATCTTAGTGCAAATGGCGATACACGTTATACA 2367
829 leSerIleLeuGlyGlyAsnValThrLeuGlyGly..... 840
2368 GTCAGCCACAACGCCACCCAAAACGGCAACCTTAGCCTCGTGGGCAATGC 2417
841 .....GlnAsnSerSerSerSerIleThrGlyAsn.. 850
2418 CCAAGCAACATTTAATCAAGCC.....ACATTAAACGGCAACACAT 2458
851 ....IleThrIleGluLysAlaAlaAsnValThrLeuGluAlaAsnAsnA 866
2459 CGGCTTCGGGCAATGCTTCATTTAATCTAAGCGACCACGCCGTACAAAAC 2508
866 laProAsnGlnGln.....AsnIleArgAspArgValIleLysLeu 879
2509 GGCAGTCTGACGCTTTCCGGCAACGCTAAGGCAAACGTAAGCCATTCCGC 2558
880 GlySerLeuLeuValAsnGlySerLeuSerLeuThrGlyGluAsnAlaAs 896
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953 953
2800 CGCCGTTCGCGCCGTTCGCGCCGTTCCCTATTATCCGT....TACACCGC 2845
954 ...HisAlaLysArgAsnGlnArgSerIleIleGlyGlyAspIleIleAs 969
2846 CAACTTCGGTAGAATCCCGTTTCAACACGCTGACGGTAAACGGCAAATTG 2895
969 nLysLysGlySerLeuAsnIleThrAspSerAsnAsnAspAlaGluIleG 986
2896 AACGGTCAGGGAACATTCCGCTTTATGTCGGAACTCTTCGGCTACCGCAG 2945
986 lnIleGlyGlyAsnIleSerGlnLysGluGlyAsnLeuThrIle.SerSe 1002
2946 CGACAAATTGAAGCTGGCGGAAAGTTCCGAAGGCACTTACACCTTGGCGG 2995
1002 rAspLysIleAsnIleThr..... 1008
2996 TCAACAATACCGGCAACGAACCTGCAAGCCTCGAACAATTGACGGTAGTG 3045
1009 .....LysGlnIleThrIleLys 1014
3046 GAAGGAAAAGACAACAAACCGCTGTCC.....GAAAACCTTAA 3083
1015 LysGlyIleAspGlyGluAspSerSerSerAspAlaThrSerAsnAlaAs 1031
3084 TTTCACCCTGCAAAACGAACACGTCGAT.....G 3112
1031 nLeuThrIleLysThrLysGluLeuLysLeuThrGluAspLeuSerIleS 1048
3113 CCGGCGCGTGGCGTTACCAACTCATCCGCAAAGACGGC...GAGTTCCGC 3159
1048 erGlyPheAsnLysAlaGluIleThrAlaLysAspGlyArgAspLeuThr 1064
3160 CTGCATAATCCGGTCAAAGAACAAGAGCTTTCCGACAAACTCGGCAAGGC 3209
1065 IleGlyAsnSer.....AsnAspGlyAsnSerGlyAl 1075
3210 AGAAGCCAAAAAACAGGCGGAAAAAGACAACGCGCAAAGCCTTGACGCGC 3259
1075 aGluAla...LysThrValThrPheAsnAsnValLys.....AspSerL 1089
3260 TGATTGCGGCCGGGCGCGATGCCGTCGAAAAGACAGAAAGCGTTGCCGAA 3309
1089 ysIleSerAlaAspGlyHisAsnValThrLeuAsnSerLysValLysThr 1105
3310 CCGGCCCGGCAGGCAGGCGGGGAAAATGTCGGCATTATGCAGGCGGAGGA 3359
1106 SerSerSerAsnGlyGlyArgGluSer..... 1114
3360 AGAGAAAAAACGGGTGCAGGCGGATAAAGACACCGCCTTGGCGAAACAGC 3409
1115 .....AsnSerAspAsnAspThrGlyLeu..... 1122
3410 GCGAAGCGGAAACCCGGCCGGCTACCACCGCCTTCCCCCGCGCCCGCCGC 3459
1123 .....ThrIleThrAlaLysAsnValGlu 1130
3460 GCCCGCCGGGATTTGCCGCAACTGCAACCCCAACCGCAGCCCCAACCGCA 3509
1131 ValAsnLysAspIleThrSerLeu..... 1138
3510 GCGCGACCTGATCAGCCGTTATGCCAATAGCGGTTTGAGTGAATTTTCCG 3559
1139 .....LysThrValAsnIleThrAlaSerGluLysValT 1150
3560 CCACGCTCAACAGCGTTTTCGCCGTACAGGACGAATTAGACCGCGTATTT 3609
1150 hrThr.ThrAlaGlySerThrIleAsnAlaThrAsnGlyLysAlaSerIl 1166
3610 GCCGAAGACCGCCGCAACGCCGTTTGGACAAGCGGCATCCGGGACACCAA 3659
1166 eThrThrLysThrGlyAspIleSerGlyThrIleSerGlyAsnThrValS 1183
3660 ACACTACCGTTCGC...AAGATTTCCGCGCCTACCGCCAACAAACCGACC 3706

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1183 erValSerAlaThrGlyAspLeuThrThrLysSerGlySerLysIleGlu 1199

3707 TGCGCCAAATCGGTATGCAGAAAAACCTCGGCAGCGGGCGCGTCGGCATC 3756
     :::   ::::::   ::::::   |||||||||:::|||:::   :::::
1200 AlaLysSerGlyGluAlaAsnValThrSerAlaThrGlyThrIleGlyGl 1216

3757 CTGTTTTCGCACAACCGGACCGAAAACACCTTCGACGACGGCATCGGCA. 3805
     :         |||   ::   :::|||   ::::::||||||:::|||
1216 y.........ThrIleSerGlyAsnThrValAsnValThrAlaAsnAlaG 1230

3806 ................................ACTCGGCACGGCTTG 3820
                                     :::   :::|||
1230 lyAspLeuThrValGlyAsnGlyAlaGluIleAsnAlaThrGluGlyAla 1246

3821 CCCACGGCGCCGTTTTCGGGCAATACGGCATCGACA......GGTTCTAC 3864
       |||         :::||||||||||   :::|||      ||||||::
1247 AlaThrLeuThrAlaThrGlyAsnThrLeuThrThrGluAlaGlySerSe 1263

3865 ATCGGCATCAGCGCGGGCGCGGGTTTTAGCAGCGGCAGCCTTTCAGACGG 3914
     :   :::|||:::::::::::::|||      |||      |||::::
1263 rIleThrSerThrLysGlyGlnValAspLeuLeuAla......GlnAsnG 1278

3915 CATCGGAGGCAAAATCCGCCGCCGCGTGCTGCATTACGGCATTCAGGCAC 3964
     ::|||   |||   |||      |||:::   :::|||
1278 lySerIleAlaGlySerIleAsnAlaAlaAsnValThrLeuAsnThrThr 1294

3965 GATACCGCGCCGGTTTCGGCGGATTCGGCATCGAACCGCACATCGGCGCA 4014
       |||      :::   |||   |||      :::   |||||||:::
1295 GlyThrLeuThrThrValAlaGlySerAspIleLysAlaThrSerGlyTh 1311

4015 ACGCGCTATTTCGTCCAAA 4033
       :::|||::::::|||
1311 rLeuValIleAsnAlaLys 1317
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seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1997.DAT:AAW30291

seq_documentation_block:

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ID   AAW30291 standard; Protein; 1598 AA.
XX
AC   AAW30291;
XX
DT   14-APR-1998  (first entry)
XX
DE   Non-typeable Haemophilus high mol.wt. surface protein HMW3.
XX
KW   Non-typeable Haemophilus; high molecular weight surface protein;
KW   HMW3; immunogen; vaccine; otitis media.
XX
OS   Haemophilus influenzae strain 5.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 113
FT                   /note= "encoded by GTG"
FT   Misc-difference 864
FT                   /note= "encoded by TGT"
XX
PN   WO9736914-A1.
XX
PD   09-OCT-1997.
XX
PF   01-APR-1997;   97WO-US04707.
XX
PR   01-APR-1996;   96US-0617697.
XX
PA   (BARE/) BARENKAMP S J.
XX
PI   Barenkamp SJ;
XX
DR   WPI; 1997-503038/46.
DR   N-PSDB; AAT90992.
XX
PT   High molecular weight proteins of non-typeable Haemophilus
PT   influenzae - useful for vaccine production
XX
PS   Claim 1; Page 93-97; 183pp; English.
XX
CC   This protein comprises the high molecular weight surface protein
CC   HMW3 (125 kDa) of non-typeable Haemophilus influenzae strain 5 that
CC   has the immunological ability to protect against disease caused by
CC   a non-typeable Haemophilus strain and is characterised by at least
CC   one surface-exposed B-cell epitope that is recognised by monoclonal
CC   antibody AD6.  The HMW3 amino acid sequence was deduced from an
CC   isolated hmw3 gene (see AAT90992).  HMW1 (see AAW30293), HMW2 (see
CC   AAW30294) and HMW4 (see AAW30292) have also been identified.  A
CC   conjugate comprising HMW3 linked to an antigen, hapten or
CC   polysaccharide, and a synthetic peptide of 6-150 amino acids
CC   corresponding to at least protective epitope of HMW3 are also
CC   claimed.  HMW proteins, conjugates and peptides can be used in
CC   vaccines, as immunogens for preparation of antibodies and as
CC   antigens for detection of these antibodies.
XX
SQ   Sequence   1598 AA;
```

alignment_scores:

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            Quality:  281.50              Length:   1497
              Ratio:  0.398                 Gaps:     73
 Percent Similarity:  47.295   Percent Identity: 20.574
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alignment_block:

US-09-303-518D-649 x AAW30291 ..

Align seg 1/1 to: AAW30291 from: 1 to: 1598

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163 CGCGACTTTGCCGAAAATAAAGGCAAGTTTGCAGTCGGGGCGAAAGATAT 212
    :::|||        |||   :::   |||:::::::::::::   |||||
158 LysAspAlaIleIleAsnThrAsnGlyPheThrAlaSerThrLeuAspIl 174

213 TGAGGTTTACAACAAAAAAGGGGAGTTGGTCGGCAAATCAATGACAAAA. 261
    |:::      |||   |||::::::                 ::::::||||||
174 eSerAsnGluAsnIleLysAlaArgAsnPheThrLeuGluGlnThrLysA 191

262 ..........GCCCCGATGATTGATTTTTCTGTG......GTGTCGCGT 294
              |||   :::::::::   ::::::      |||::::::
191 spLysAlaLeuAlaGluIleValAsnHisGlyLeuIleThrValGlyLys 207

295 AACGGCGTGGCGGCATTGGTGGGC............GATCAATATATTGT 332
    :::|||   :::   |||:::|||            ::::::   :::::
208 AspGlySerValAsnLeuIleGlyGlyLysValLysAsnGluGlyValIl 224

333 GAGCGTGGCACATAACGGCGGCTATAACAACGTTGATTTTGGTGCGGAAG 382
    :||||||      |||||||||      ::::::::: |||:::
224 eSerVal......AsnGlyGly......SerIleSer.LeuLeuAlaGly 236

383 GAAGAAATCCCGATCAACATCGTTTTACTTATAAAATTGTGAAACGGAAT 432
    :::::::|||   |||:::   ::::::          :::      :::|||
237 GlnLysIleThrIleSerAspIleIleAsnProThrIleThrTyrSerIl 253

433 AATTATAAAGCAGGGACTAAAGGCCATCCTTATGGCGGCGATTATCATAT 482
    |         :::
253 eAlaAlaProGlu..................................... 257

483 GCCGCGTTTGCATAAATTTGTCACAGATGCAGAACCTGTTGAAATGACCA 532
      :::   :::|||||||||:::::
258 ..AsnGluAlaIleAsnLeuGlyAsp....................... 265

533 GTTATATGGATGGGCGGAAATATATCGATCAAAATAATTACCCTGACCGT 582
    ::::::      ||||||||||||:::::::::      |||:::
266 IlePheAlaLysGlyGlyAsnIleAsnValArgAlaAlaThrIleArg.. 281

583 GTTCGTATTGGGGCAGGCAGGCAATATTGGCGATCTGAT.GAAGATGAGC 631
                              |||   |||   |||      |||:::
282 .....................AsnLysGlyLysLeuSerAlaAspServ 291

632 CCAATAACCGCGAAAGTTCATATCATATTGCAAGTGCGTATTCTTGG... 678
      ::::::   :::|||:::      :::   ||||||   :::
```

```
 291 alSerLysAspLysSerGlyAsnIleValLeuSerAlaLysGluGlyGlu 307

 679 ...CTCGTTGGTGGCAATACCTTTGCACAAAAT..................  708
          :::|||||||         |||||||||
 308 AlaGluIleGlyGlyValIleSerAlaGlnAsnGlnGlnAlaLysGlyGl  324

 708 ....................................................  708

 324 yLysLeuMetIleThrGlyAspLysValThrLeuLysThrGlyAlaValI  341

 709 ..........GGATCAGGTGGTGGCACAGTCAACTTAGGTAGTGAAAAA  747
                |||:::   ||||||   :::   |||||||||||||
 341 leAspLeuSerGlyLysGluGlyGlyGluThrTyrLeuGlyGlyAspGlu  357

 748 ATTAAACATAGCCCATATGGTTTT.....................TTACC  776
          ::::::      |||:::                      |||
 358 ArgGlyGluGlyLysAsnGlyIleGlnLeuAlaLysLysThrThrLeuGl  374

 777 AACAGGAGGCTCATTTGGCGACAGTGGCTCACCAATGTTTATCTATGATG  826
       |||||||||||||   ||||||
 374 uLysGlySerThrIleAsnValSerGly.....................  383

 827 CCCAAAAGCAAAAG..................TGG............TTA  846
          |||:::|||                  |||            |||
 384 .....LysGluLysGlyGlyArgAlaIleValTrpGlyAspIleAlaLeu  398

 847 ATTAATGGGGTATTGCAAACGGGCAACCCCTATATAGGAAAAAGCAATGG  896
     |||:::|||   :::::::::   :::      |||:::|||:::::::||
 399 IleAspGlyAsnIleAsnAlaGlnGlyLysAspIleAlaLysThrGlyGl  415

 897 CTTC.....................................CAGCTGG  907
     ||||                                      :::|
 415 yPheValGluThrSerGlyHisTyrLeuSerIleAspAspAsnAlaIleV  432

 908 TTCGT...AAAGATTGGTTCTATGATGAAATCTTTGCTGGAGATACCCAT  954
     ||:::   |||:::|||:::                  |||   :::
 432 alLysThrLysGluTrpLeuLeu.................AspProGlu  442

 955 TCAGTATTCTACGAACCACGTCAAAATGGGAAATACTCTTTTAACGACGA 1004
     :::|||      |||      :::   ::::::   :::::::::   ||
 443 AsnValThrIleGluAlaProSerAlaSerArgValGluLeuGlyAlaAs  459

1005 TAATAATGGCACAGGA............AAAATCAATGCCAAACATGAAC 1042
     |:::|||:::   :::           |||::::::   |||   ::::
 459 pArgAsnSerHisSerAlaGluValIleLysValThrLeuLysLysAsnA  476

1043 ACAATTCTCTGCCTAATAGATTAAAAACACGAACCGTTCAATTGTTTAAT 1092
     :::::||||||
 476 snThrSerLeu.....................................  479

1093 GTTTCTTTATCCGAGACAGCAAGAGAACCTGTTTATCATGCTGCAGGTGG 1142
     :::::::|||:::::::|||:::   :::   :::      :::|||
 480 ThrThrLeuThrAsnThrThrIleSerAsnLeuLeuLysSerAlaHisVa  496

1143 TGTCAAC...AGTTATCGACCCAGACTGAATAATGGAGAAAATATTTCCT 1189
      ||||||   :::   |||   :::|||:::   ::::::::::||||||
 496 lValAsnIleThrAlaArgArgLysLeuThrValAsnSerSerIleSer.  512

1190 TTATTGACGAAGGAAAAGGCGAATTGATACTTACCAGCAACATCAATCAA 1239
       |||::::::|||   ::::::|||||||||   |||:::   :::|||
 513 ..IleGluArgGly...SerHisLeuIleLeuHisSerGlu...GlyGln  526

1240 GGTGCTGGAGGATTATATTTCCAAGGAGATTTTACGGTCTCGCCTGAAAA 1289
     |||:::   |||:::   ::::::   |||:::|||   :::      ||
 527 GlyGlyGlnGlyValGlnIleAspLysAspIleThrSerGluGlyGlyAs  543

1290 TAACGAAACTTGGCAAGGCGCGGGCGTTCATATCAGTGAAGACAGTACC. 1338
     |         ::::::|||:::   |||   :::   ::::::   |||
 543 nLeuThrIleTyrSerGlyGlyTrpValAspValHisLysAsnIleThrL  560

1339 ...................GTTACTTGGAAAGTAAACGGCGTGGCAAAC 1368
                        :::|||   |||   :::   :::|||
 560 euGlySerGlyPheLeuAsnIleThrThrLysGluGlyAspIleAlaPhe  576

1369 GACCGCCTGTCCAAAATCGGCAAAGGCACGCTGCACGTTCAAGCCAAAGG 1418
     :::      :::|||   |||::::::::::|||   :::   |||
  577 Glu......AspLysSerGlyArgAsnAsnLeuThrIleThrAla.....  589

1419 GGAAAACCAAGGCTCGATCAGCGTGGGC......GACGGTACAGTCATTT 1462
            ||||||:::|||:::   |||      :::|||      :::
  590 .......GlnGlyThrIleThrSerGlyAsnSerAsnGlyPheArgPheA  604

1463 TGGATCAGCAGGCAGACGATAAAGGCAAAAAACAAGCCTTTAGTGAAATC 1512
       :::   :::   ::::::   |||   |||   :::|||:::::
  604 snAsnValSerLeuAsnSerLeuGlyGlyLysLeuSerPheThrAspSer  620

1513 GGCTTGGTCAGCGGCAGGGGTACGGTGCAACTGAATGCCGATAATCAGTT 1562
                |||||   |||   :::   |||   :::|||:::||
  621 ArgGluAspArgGlyArgArgThr...LysGlyAsnIleSerAsnLysPh  636

1563 CAACCCCGACAAACTCTATTTCGGCTTTCGCGGCGGACGTTTGGATTTAA 1612
     |:::                                |||   |||:::::::
  636 eAsp.............................GlyThrLeuAsnIleS  643

1613 ACGGGCAT.........TCGCTTTCG.................TTCCAC 1635
     ::|||            |||::::::                 |||:::
  643 erGlyThrValAspIleSerMetLysAlaProLysValSerTrpPheTyr  659

1636 CGTATTCAAAATACCGATGAAGGGGCGATGATTGTCAACCACAATCAAGA 1685
     |||            |||:::|||            |||
  660 Arg............AspLysGlyArgThrTyrTrpAsn...........  668

1686 CAAAGAATCCACCGTTACCATTACAGGC............AATAAAGATA 1723
            :::|||:::::::::|||:::            |||   :::|
  669 ....ValThrThrLeuAsnValThrSerGlySerLysPheAsnLeuSerI  684

1724 TTGCTACAACCGGCAATAACAACAGCTTGGATAGCAAAAAAGAAATTGCC 1773
     ||   :::||||||:::::::::::      |||   ::::::
  684 leAspSerThrGlySerGlySerThrGlyProSerIleArgAsnAlaGlu  700

1774 TACAACGGTTGGTTTGGCGAGAAAGATACG.................AC 1805
        ||||||      :::|||   |||                    ::
  701 LeuAsnGlyIleThrPheAsnLysAlaThrPheAsnIleAlaGlnGlySe  717

1806 CAAAACGAACGGGCGGCTCAACCTTGTTTACCAGCCC............. 1842
     :   :::|||      ::::::         :::|||
  717 rThrAlaAsnPheSerIleLysAlaSerIleMetProPheLysSerAsnA  734

1843 ........GCCGCAGAAGACCGCACCCTGCTGCTTTCCGGCGGAACAAAT 1884
             |||      ::::::   :::   ::::||||||||   :::
  734 laAsnTyrAlaLeuPheAsnGluAspIleSerValSerGlyGlyGlySer  750

1885 TTAAACGGCAACATCACGCAAACAAACGGCAAACTGTTTTTCAGCGGCAG 1934
     ||||||   :::::::::   ::::::::::::::::
  751 LeuAsnPheLysLeuAsnAlaSerSerSerAsnIle.............  762

1935 ACCAACACCGCACGCCTACAATCATTTAAACGACCATTGGTCGCAAAAAG 1984
       ||||||
  763 .GlnThrPro.....................................  765

1985 AGGGCATTCCTCGCGGGGAAATCGTGTGGGACAACGACTGGATCAACCGC 2034
                |||   |||:::
  766 ..............GlyValIleIle.....................  769

2035 ACATTTAAAGCGGAAAACTTCCAAATTAAAGGCGGACAGGCGGTGGTTTC 2084
          |||::::::||||||::::::::::||||||::::::::::
  770 ......LysSerGlnAsnPheAsnValSerGlyGlySerThrLeuAsnLe  784

2085 CCGCAATGTTGCCAAAGTGAAAGGCGATTGGCATTTGAGCAATCACGCCC 2134
       :::      ::::::::::::      :::   ::::::|||      :
  784 uLysAlaGluGlySerThrGluThrAlaPheSerIleGluAsnAspLeuA  801

2135 AAGCAGTTTTTGGTGTCGCACCGCATCAAAGCCACACAATCTGTACACGT 2184
     ::
  801 sn.....................................................  801
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     1286 uValAlaThrGlyAlaThrLeuAlaValGlyAsnIleSerGlyAsnThrV 1303

     3845 ........ACGGCATCGACAGGTTCTACATCGGCATCAGCGCGGGCGCGG 3886
                  ||||||::::::|||:::   ::::::::::::   :::
     1303 alThrIleThrAlaAspSerGlyLysLeuThrSerThrValGlySerThr 1319

     3887 GTTTTAGCAGCGGCAGCCTTTCAGACGGCATCGGAGGCAAAA........ 3928
          :::   ::::::   :::      |||:::|||::::::
     1320 IleAsnGlyThrAsnSerValThrThrSerSerGlnSerGlyAspIleGl 1336

     3929 .........TCCGCCGCCGCGTGCTGCATTACGGCATTCAGGCACGAT. 3967
                  |||:::   :::      :::||||||         |||
     1336 uGlyThrIleSerGlyAsnThrValAsnValThrAlaSerThrGlyAspL 1353

     3968 ..ACCGCGCCGGTTTCGGCGGATTCGGCATCGAACCGCACATCGGCGCAA 4015
            |||         ||||||          :::::::::   :::|||
     1353 euThrIleGlyAsnSerAlaLysValGluAlaLysAsnGlyAlaAlaThr 1369

     4016 CGCGCTATTTCGTCCAAAAAGCGGATTACCGCTACGAAAACGTCAATATC 4065
            :::   :::|||   |||      |||   |||   :::|||||::
     1370 LeuThrAlaGluSerGlyLysLeuThrThrGlnThrGlySerSerIleTh 1386

     4066 GCCACCCCCGGCCTTGCATTCAACCGCTACCGCGCGG 4102
          :         :::   ::::::|||   ||||||:::
     1386 rSerSerAsnGly...GlnThrThrLeuThrAlaLys 1397

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seq_documentation_block:
ID   AAR41731 standard; Protein; 1338 AA.
XX
AC   AAR41731;
XX
DT   26-APR-1994  (first entry)
XX
DE   High molecular weight protein 3 (HMW3).
XX
KW   HMW; high molecular weight protein; virus; vaccine; influenza;
KW   epitope; immunity; haemophilus influenzae.
XX
OS   Haemophilus influenzae.
XX
PN   WO9319090-A.
XX
PD   30-SEP-1993.
XX
PF   16-MAR-1993;   93WO-US02166.
XX
PR   16-MAR-1992;   92GB-0005704.
XX
PA   (BARE/) BARENKAMP S J.
PA   (INRM ) INSERM INST NAT SANTE & RECH  MEDICALE.
XX
PI   Barenkamp SJ;
XX
DR   WPI; 1993-320683/40.
DR   N-PSDB; AAQ49510.
XX
PT   High molecular weight surface proteins - of non-typeable
PT   haemophilus which exhibit immunogenic properties
XX
PS   Claim 5; Figure 10; 100pp; English.
XX
CC   The isolation and purification of the high molecular weight protein
CC   enables the identification of the major protective epitopes of the
CC   protein by conventional epitope mapping.  These epitopes can then be
CC   synthesised using standard techniques and incorporated into fully
CC   synthetic or recombinant vaccines.
XX
SQ   Sequence   1338 AA;


alignment_scores:
                Quality:  281.00              Length:   1478
                  Ratio:  0.404                 Gaps:     72
  Percent Similarity:  47.023   Percent Identity: 20.162

alignment_block:
 US-09-303-518D-649 x AAR41731   ..

 Align seg 1/1  to: AAR41731  from: 1  to: 1338

     127 GGACACACTTATTTCGGCATCAACTACCAATACTATCGCGACTTTGCCGA 176
         |||:::||||||:::|||                          :::::
      89 GlyGluThrTyrLeuGly.........................GlyAs 96

     177 AAATAAAGGCAAGTTTGCAGTCGGGGCGAAAGATATTGAGGTTTACAACA 226
         :::::::|||:::          |||   :::   |||::::::   :::|
      96 pGluArgGlyGlu.........GlyLysAsnGlyIleGlnLeuAlaLysL 110

     227 AAAAAGGGGAGTTGGTCGGCAAATCAATGACAAAAGCCCCGATGATTGAT 276
         ||                        ::::::   |||:::      |||:::
     110 ys..................ThrThrLeuGluLysGlySerThrIleAsn 120

     277 TTTTCTGTGGTGTCGCGTAACGGCGTGGCGGCATTGGTGGGCGATCAATA 326
            |||      :::::::::|||   |||   :::   ||||||
     121 ValSerGlyLysGluLysGlyGlyArgAlaIleValTrpGlyAspIleAl 137

     327 TATTGTG..........................AGCGTGGCACATAACG 349
          ::::::                         :::::::|||   :::|
     137 aLeuIleAspGlyAsnIleAsnAlaGlnGlyLysAspIleAlaLysThrG 154

     350 GCGGCTAT..................................... 357
         |||||:::
     154 lyGlyPheValGluThrSerGlyHisTyrLeuSerIleAspAspAsnAla 170

     357 ..... 357

     171 IleValLysThrLysGluTrpLeuLeuAspProGluAsnValThrIleGl 187

     358 .............AACAACGTTGATTTTGGTGCGGAAGGAAGAAATCCCG 394
                     :::::::|||::::::||||||:::   ||||||
     187 uAlaProSerAlaSerArgValGluLeuGlyAlaAsp...ArgAsnSerH 203

     395 ATCAACATCGTTTTACTTATAAAATTGTGAAACGGAATAATTATAAAGCA 444
           :::   :::              :::|||:::||||||   :::
     203 isSerAlaGluValIleLysValThrLeuLysLysAsnAsnThrSerLeu 219

     445 GGGACTAAAGGCCATCCTTATGGCGGCGATTATCATATGCCGCGTTTGCA 494
         |||      :::                                 :::
     220 ThrThrLeuThrAsn.......................ThrThrIleSe 228

     495 TAAATTTGTCACAGATGCAGAACCTGTTGAAATGACCAGT.......... 534
          :::::::::   :::|||:::   |||::::::|||:::
     228 rAsnLeuLeuLysSerAlaHisValValAsnIleThrAlaArgArgLysL 245

     535 ..TATATGGATGGGCGGAAATATATCGATCAAAATAATTACCCTGACCGT 582
             :::::::::          |||:::::::::::::::
     245 euThrValAsnSerSerIleSerIleGluArgGlySerHisLeuIleLeu 261

     583 GTTCGTATTGGGGCAGGCAGGCAATATTGGCGATCTGATGAAGATGAGCC 632
                 |||   |||   |||       :::   |||:::|||
     262 HisSerGluGlyGlnGlyGlyGlnGlyValGlnIleAspLysAsp..... 276

     633 CAATAACCGCGAAAGTTCATATCATATTGCAAGTGCGTATTCTTGGCTCG 682
                                |||:::|||
     277 .......................IleThrSerGlu............. 280

     683 TTGGTGGCAATACCTTTGCACAAAATGGATCAGGTGGT............ 720
          |||||||||                |||||||||
     281 ..GlyGlyAsnLeuThrIleTyr......SerGlyGlyTrpValAspVal 294

     721 ...GGCACAGTCAACTTAGGTAGTGAAAAAATTAAACATAGCCCATATGG 767
            :::::::::|||||||||                          ||
     295 HisLysAsnIleThrLeuGlySer.......................Gl 303
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```
 826 sIleSerThrAsp...GlyHisAsnValThrLeuAsnSerGlu..... 839

2303 TAAATCTCACAGGGCTTGCCACACTCAACGGCAATCTTAGTGCAAATGGC 2352
                  :::   |||   |||||||:::   :::|||:::::: 
 840 .............ValLysThrSerAsnGlySerSerAsnAlaGlyAsn 851

2353 GAT......ACACGTTATACAGTCAGC...CACAACGCCACCCAAAACGG 2393
     |||      |||      |||:::|||      ::::::|||   |||:: 
 852 AspAsnSerThrGlyLeuThrIleSerAlaLysAspValThrValAsnAs 868

2394 CAACCTTAGCCTCGTGGGCAATGCCCAAGCAACATTTAATCAAGCCACAT 2443
     :|||::::::            ::::::   |||:::|||   :::::: 
 868 nAsnValThr............SerHisLysThrIleAsnIleSerAlaA 881

2444 TAAACGGCAACACATCGGCTTCGGGCAATGCTTCATTTAATCTAAGCGAC 2493
       ||||||:::::::::::::   :::::::::::|||   ::: 
 881 laAlaGlyAsnValThrThrLysGluGlyThrThrIleAsnAlaThrThr 897

2494 CACGCCGTA............CAAAACGGCAGTCTGACGCTTTCCGGCAA 2531
        :::|||             |||||||||      |||:::::|||||
 898 GlySerValGluValThrAlaGlnAsnGly......ThrIleLysGlyAs 912

2532 C...GCTAAGGCAAACGTAAGCCATTCCGCACTCAACGGTAATGTCTCCC 2578
     |   ::::::   ||||||:::   :::|||   :::   |||::: 
 912 nIleThrSerGlnAsnValThrValThrAlaThrGlu...AsnLeuValT 928

2579 TAGCCGATAAGGCAGTATTCCATTTTGAAAGC.............AGC 2613
       :::::::::||||||::::::      |||              ||| 
 928 hrThrGluAsnAlaValIleAsnAlaThrSerGlyThrValAsnIleSer 944

2614 CGCTTTACCGGACAAATCAGCGGCGGCAAGGATACGGCA.........TT 2654
           ||||||:::|||:::||||||   :::::::::      :: 
 945 ThrLysThrGlyAspIleLysGlyGlyIleGluSerThrSerGlyAsnVa 961

2655 ACACTTAAAAGACAGCGAATGGACGCTGCCGTCAGGCACGGAATTAGGCA 2704
     :::::::      |||      ||||||           ::::::::::| 
 961 lAsnIleThrAlaSerGlyAsnThrLeu............LysValSerA 974

2705 ATTTAAACCTTGACAACGCCACCATTACACTCAATTCCGCCTATCGCCAC 2754
     ||::::::   ::::::::::|||:::|||   ::: 
 974 snIleThrGlyGlnAspValThrValThrAlaAsp.............. 985

2755 GATGCGGCAGGGGCGCAAACCGGCAGTGCGACAGATGCGCCGCGCCGCCG 2804
           |||||||||   |||   :::||| 
 986 ......AlaGlyAlaLeuThrThrThrAla..................... 993

2805 TTCGCGCCGTTCGCGCCGTTCCCTATTATCCGTTACACCGCCAACTTCGG 2854
                        |||   :::|||:::|||      :::::: 
 994 ...............GlySerThrIleSerAlaThrThrGlyAsnAla. 1004

2855 TAGAATCCCGTTTCAACACGCTGACGGTAAACGGCAAATTGAACGGTCAG 2904
                  |||      |||   :::|||   :::|||||::: 
1005 .............AsnIleThrThrLysThrGlyAspIleAsnGlyLys 1016

2905 GGAACATTCCGCTTTATGTCGGAACTCTTCGGCTACCGCAGCGACAAATT 2954

1016 ..................................................... 1016

2955 GAAGCTGGCGGAAAGTTCCGAAGGCACTTACACCTTGGCGGTCAACAAT. 3003
          :::||||||||||:::|||:::   ||||||:::::::::::::  
1017 .......ValGluSerSerSerGlySerValThrLeuValAlaThrGlyA 1031

3004 ...........ACCGGCAACGAACCTGCAAGCCTCGAACAATTGACGGTA 3042
               :::||||||      ::::::          :::|||::: 
1031 laThrLeuAlaValGlyAsnIleSerGlyAsnThrValThrIleThrAla 1047

3043 GTGGAAGGAAAAGACAACAAACCGCTGTCCGAAAACCTTAAT........ 3084
     :::||||||   ::::::   :::::::::::::::||| 
1048 AspSerGlyLysLeuThrSerThrValGlySerThrIleAsnGlyThrAs 1064

3085 .....................................TTCACCCTGCAAA 3097
                                           |||:::::::  
1064 nSerValThrThrSerSerGlnSerGlyAspIleGluGlyThrIleSerG 1081

3098 ACGAACACGTCGATGCCGGCGCGTGGCGTTACCAACTCATCCGCAAAGAC 3147
     :::::   |||:::::::   |||                     ::: 
1081 lyAsnThrValAsnValThrAla.....................SerThr 1090

3148 GGCGAGTTCCGCCTGCATAATCCGGTCAAAGAACAAGAGCTTTCCGACAA 3197
     |||::::::   :::   |||   :::|||          ::::::   || 
1091 GlyAspLeuThrIleGlyAsnSerAlaLys.........ValGluAlaLy 1104

3198 ACTCGGCAAGGCAGAAGCCAAAAAACAGGCGGAAAAAGACAACGCGCAAA 3247
     |   |||   |||              ::::::   |||   :::::::|||: 
1104 sAsnGlyAlaAlaThrLeuThrAlaGluSerGlyLysLeuThrThrGlnT 1121

3248 GCCTTGACGCGCTGATTGCGGCCGGGCGCGATGCCGTCGAAAAGACAGAA 3297
     ::   :::::::::   :::::::::                ::::|||
1121 hrGlySerSerIleThrSerSerAsn............GlyGlnThrThr 1133

3298 AGCGTTGCCGAACCGGCCCGGCAGGCAGGCGGGGAAAAT........... 3336
        :::|||:::   :::      ||||||:::   ||| 
1134 LeuThrAlaLysAspSerSerIleAlaGlyAsnIleAsnAlaAlaAsnVa 1150

3337 .............GTCGGCATTATGCAGGCGGAGGAAGAGAAAAAACGGG 3373
                    :::|||   :::   :::      ::::::|||   : 
1150 lThrLeuAsnThrThrGlyThrLeuThrThrThrGlyAspSerLys...I 1166

3374 TGCAGGCGGATAAAGACACCGCCTTGGCGAAACAGCGCGAAGCGGAAACC 3423
     :::::|||   :::   |||          :::   :::::::|||::: 
1166 leAsnAlaThrSerGlyThrLeuThrIleAsnAlaLysAspAlaLysLeu 1182

3424 CGGCCGGCTACCACCGCCTTCCCCCGCGCCCGCCGCGCCCGCCGGGATTT 3473
           |||:::::::::: 
1183 AspGlyAlaAlaSerGly.............................. 1188

3474 GCCGCAACTGCAACCCCAACCGCAGCCCCAACCGCAGCGCGACCTGATCA 3523
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1189 ................................AspArgThrValValA 1194

3524 GCCGTTATGCCAATAGCGGTTTGAGTGAATTTTCCGCCACGCTCAACAGC 3573
     ::            ||||||   ::::::   :::|||      :::||| 
1194 snAlaThrAsnAlaSerGlySerGlyAsnValThrAlaLysThrSerSer 1210

3574 GTTTTCGCCGTACAGGACGAATTAGAC..............CGCGTATT 3608
                  :::      :::|||:::                :::::::: 
1211 SerValAsnIleThrGlyAspLeuAsnThrIleAsnGlyLeuAsnIleIl 1227

3609 TGCCGAAGACCGCCGCAACGCCGTTTGGACAAGCGGCATCCGG...GACA 3655
     ::::|||:::   ||||||:::|||          |||   :::   |||: 
1227 eSerGluAsnGlyArgAsnThrValArgLeuArgGlyLysGluIleAspV 1244

3656 CCAAACACTACCGTTCGCAAGATTTCCGCGCCTACCGCCAACAAACCGAC 3705
     ::|||:::          |||    ::::::   :::::::::::: 
1244 alLysTyrIle......GlnPro.GlyValAlaSerValGluGluValIl 1258

3706 CTGCGCCAAATCGGTATGCAGAAAAACC..................... 3733
          ||||||   |||   :::|||::: 
1258 eGluAlaLysArgValLeuGluLysValLysAspLeuSerAspGluGluA 1275

3734 .....TCGGCAGCGGGCGCGTCGGCATCCTGTTTTCGCACAACCGGACCG 3778
          :::   |||      ::::::|||:::   |||   :::   ||| 
1275 rgGluThrLeuAlaLysLeuGlyValSerAlaValArgPheValGluPro 1291

3779 AAAACACCTTCGACGACGGCATCGGCAACTCGGCACGGCTTGCCCACGGC 3828
     ::::::      |||:::          |||::::::   :::   ||| 
1292 AsnAsnAlaIleThrVal......AsnThrGlnAsnGluPheThrThrLy 1306

3829 GCCGTTTTCGGGCAATACGGCATCGACAGGTTCTACA......TCGGCAT 3872
      |||   |||      |||   |||   |||::::::      |||:::: 
1306 sProSerSerGlnValThrIleSerGluGlyLysAlaCysPheSerSerG 1323

3873 CAGCGCGGGCGCGGGTTTTAGCAGCGGCAGCC 3904
     ::      |||||||||   :::   :::||| 
1323 lyAsnGlyAlaArgValCysThrAsnValAla 1333
```

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seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2000.DAT:AAB01827

seq_documentation_block:
ID   AAB01827 standard; Protein; 969 AA.
XX
AC   AAB01827;
XX
DT   11-SEP-2000  (first entry)
XX
DE   Haemophilus influenzae strain Joyc mature HMW2A protein, SEQ ID NO:32.
XX
KW   Mature HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW   non-typeable Haemophilus influenzae; NTHi; hon-encapsulated;
KW   recombinant production; Escherichia coli; antibacterial; vaccine;
KW   human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW   detection; diagnosis.
XX
OS   Haemophilus influenzae strain Joyc.
XX
PN   WO200020609-A2.
XX
PD   13-APR-2000.
XX
PF   07-OCT-1999;   99WO-CA00938.
XX
PR   07-OCT-1998;   98US-0167568.
PR   08-DEC-1998;   98US-0206942.
XX
PA   (CONN-) CONNAUGHT LAB LTD.
XX
PI   Loosmore SM,  Yang Y,  Klein MH;
XX
DR   WPI; 2000-303789/26.
DR   N-PSDB; AAA52178.
XX
PT   Nucleic acid molecule for producing recombinant high molecular weight
PT   proteins of Haemophilus which are used as a vaccine to provide
PT   protection against Haemophilus induced diseases in humans -
XX
PS   Claim 8; Fig 19A-O; 307pp; English.
XX
CC   The invention relates to the recombinant production of Haemophilus
CC   influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC   expression construct used to effect recombinant expression comprises a
CC   promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC   to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC   influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC   clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC   hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC   and the hmwB and hmwC genes encode accessory proteins which are
CC   responsible for post-translational processing and secretion of the HMWA
CC   proteins. The modified hmwABC operon used in the expression construct of
CC   the invention contains an A gene modified such that it encodes only the
CC   mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC   and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC   strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC   vectors are used for the production of recombinant H. influenzae HMW
CC   proteins which can be used as vaccines to mediate a humoral or
CC   cell-mediated immune response to provide protection against diseases in
CC   humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC   pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC   antigens in immunoassays for detecting antibodies against Haemophilus,
CC   HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC   HMW proteins can be used to isolate and clone hmw genes from other
CC   non-typeable strains of Haemophilus via hybridisation reactions. The
CC   present sequence represents a mature HMWA protein from a non-typeable
CC   strain of H. influenzae.
XX
SQ   Sequence   969 AA;


alignment_scores:
            Quality:  280.50            Length:   1143
            Ratio:  0.506               Gaps:     52
 Percent Similarity:  48.469   Percent Identity: 20.385

alignment_block:
 US-09-303-518D-649 x AAB01827   ..

 Align seg 1/1  to: AAB01827  from: 1  to: 969

    1090 AATGTTTCTTTATCC.................GAGACAGCAAGAGAACC 1121
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       3 AsnValSerIleGluAsnProSerThrGluArgAsnAspSerAsnGluAs 19

    1122 TGTTTATCATGCTGCAGGTGGTGTCAACAGTTATCGACCCAGACTGAATA 1171
          :::   :::::::::   |||   |||      :::|||:::::::|||||
      19 pLeuGluTyrThrGlyThrGlyGluAsnIleAsnAsnProLysValAsnA 36

    1172 ATGGA............................GAAAATATT...... 1185
         ||                               |||||||||
      36 snGlnSerLysLysThrLeuThrSerSerIleLeuGluAsnIleLeuLys 52

    1186 ......TCCTTTATTGAC...GAAGGAAAAGGCGAATTGATACTTACCAG 1226
               ||||||::::::      :::      ::::::   ::::::||
      53 LysGlySerPheValAsnIleThrAlaThrAspAsnIleTyrValAsnSe 69

    1227 CAACATCAATCAAGGT...GCTGGAGGATTATATTTCCAAGGAGATTTTA 1273
         |:::||||||   |||   :::|||   |||   :::::::|||
      69 rSerIleAsnIleGlyAspSerGlyHisLeuIleLeuSerGlyGlyGlyA 86

    1274 CGGTCTCGCCTGAAAATAACGAAACTTGGCAAGGCGCGGGCGTTCATATC 1323
                                        :::|||:::||||||   |||
      86 rg.........................AsnGlyGlyGlyValLysIle 93

    1324 AGTGAAGACAGTACCGTTACTTGGAAAGTAAACGGCGTGGCAAACGACCG 1373
         :::::::::   |||   |||
      94 AsnLysAsnIleThrSerThr.............................. 100

    1374 CCTGTCCAAAATCGGCAAAGGCACGCTGCACGTTCAAGCCAAAGGG.... 1419
                           |||:::|||   :::::::::||||||
     101 ...............GlyGlySerLeuThrIleAsnSerLysGlyTrpV 112

    1420 ..GAAAACCAAGGCTCGATCAGCGTGGGC..................... 1446
           :::   :::::::::|||||||:::|||
     112 alAspIleHisSerAsnIleSerLeuGlyThrGlyPheLeuAsnIleThr 128

    1447 ...GACGGTACAGTCATTTTGGATCAGCAGGCAGACGATAAAGGCAAAAA 1493
           :::|||:::|||   :::::::::          ||||||:::::::::
     129 SerAsnGlySerValAlaPheGluLysAlaAspLysAspLysAlaArgSe 145

    1494 ACAAGCCTTTAGTGAAATCGGCTTGGTCAGCGGCAGGGGTACGGTGCAAC 1543
         :   |||   ::::::|||           ::::::|||   ::::::|
     145 rAlaAlaAspAlaGlnIle.........ValAlaGlnGlyIleIleAsnL 159

    1544 TGAATGCCGATAATCAGTTCAACCCCGACAAACTCTATTTCGGCTTTCGC 1593
         ||:::::::::|||:::                              ||||||
     159 euThrGlyGluAsnLys.......................ThrPheArg 167

    1594 GGCGGACGTTTGGATTTAAACGGGCATTCGCTTTCGTTCCACCGTATTCA 1643
            ::::::::::::|||||||||   :::   ::::::          ::
     168 LeuAsnAsnValSerLeuAsnGlyValGlyGlnGlyLeuSerIleThrSe 184

    1644 AAATACCGATGAAGGGGCGATGATTGTCAACCACAATCAAGACAAAGAAT 1693
         :|||                  :::   |||:::::::::      ::::
     184 rAsn.................ValGlyAsnGlnThrHisLysPheAspG 195

    1694 CCACCGTTACCATTACAGGCAATAAAGATATT..............GCT 1728
         ::   ::::::||||||||||||      |||               |||
     195 lyGluIleAsnIleThrGlyAsnValThrIleAsnGlnThrAlaProAla 211

    1729 ACAACCGGCAAT...AACAACAGCTTGGAT..............AGCAA 1760
         |||||||:::      |||   |||   |||               |||
     212 ThrThrAlaTyrTrpAsnPheSerTyrAspSerTyrTrpAsnValSerTh 228

    1761 AAAAGAAATTGCCTACAACGGTTGGTTTGGCGAGAAAGATACGACCAAAA 1810
```

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      ::::::      |||:::  |||              |||:::: 
 228 rLeuAsnValGlnLysAsnSerSerPheThrPheIleLysArgThrGluS 245

1811 CGAACGGGCGGCTCAACCTTGTTTACCAGCCCGCCGCAGAAGACCGCACC 1860
     ::|||           :::  |||::::::     |||::: 
 245 erAsnArg.............PheGlyProThrThrProLeuArgSer 256

1861 CTGCTGCTTTCCGGCGGA.........ACAAATTTAAACGGCAACATC.. 1899
          |||||||||        ::::::  |||||||||::: 
 257 .........SerGlyGlyValPhePheAsnGlyThrAsnGlyAsnMetVa 270

1900 .......ACGCAAACAAACGGCAAACTGTTTTTCAGCGGCAGACCAACAC 1942
         :::  ||||||:::::::::::::|||:::  :::||| 
 270 lLeuAsnValGlyThrAsnSerArgValLeuPheAsnLeuLysPro.... 285

1943 CGCACGCCTACAATCATTTAAACGACCATTGGTCGCAAAAAGAGGGCATT 1992
                    |||::::::  ::::::::::::  ::: 
 286 ...................AsnGluAsnThrAsnAsnSerLysProLeu 295

1993 CCTCGCGGGGAAATCGTGTGGGACAACGACTGGATCAACCGCACATTTAA 2042
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 296 Pro.................................LeuGlnPheAs 300

2043 AGCGGAAAACTTCCAAATTAAAGGCGGACAGGCGGTGGTTTCCCGCAATG 2092
     :|||:::        |||  |||||| 
 300 nAlaAsnIleThrAlaIleGlyGlyGly..................... 309

2093 TTGCCAAAGTGAAAGGCGATTGGCATTTGAGCAATCACGCCCAAGCAGTT 2142
        :::|||:::  |||  |||  :::|||||::: 
 310 .....SerValSerPheAspIleHis...AlaAsnHisSer..... 320

2143 TTTGGTGTCGCACCGCATCAAAGCCACACAATCTGTACACGTTCGGACTG 2192
        |||  :::  :::  :::  :::      :::  |||||| 
 321 ...GlyArgGlyAlaGluLeuLysMetAsnThrIleAsnIleSerAspGl 336

2193 GACGGGTCTGACA.........................AATTGTG 2212
      |||:::||||||                        : 
 336 yThrSerLeuThrLeuGlnSerHisValArgLysAspSerAlaPheIleI 353

2213 TCGAAAAAACCATTACC.......................... 2229
     ::::::|||  :::||| 
 353 leSerLysAspLeuThrIleAsnAlaThrGlySerAsnPheThrLeuGlu 369

2230 ........................GACGATAAAGTGATTGCTTC 2249
                                ::::::|||:::|| 
 370 GlnSerProAspSerPheThrAspLysTyrProGlyArgAlaIleSerSe 386

2250 ATTGACTAAGACCGACATCAGC...GGCAATGTCGATCTTGCCGATCACG 2296
     |     :::      ||||||  |||||||||:::|||:::  ::: 
 386 rThrLysAsnIleThrIleSerGlyGlyAsnValSerLeuGlyGlyGln. 402

2297 CTCATTTAAATCTCACAGGGCTTGCCACACTCAACGGCAATCTTAGTGCA 2346
                 ::::::  :::  ::::::|||||::::::
 403 ............AsnSerSerSerAspIleLysGlyAsnIleThrIle 414

2347 AATGGCGATACACGTTATACAGTC...AGCCACAACGCCACCCAAAAC.. 2391
     :::::::::|||:::  |||:::  :::||||||:::  ::::::
 415 LysSerSerThrAsnValThrLeuLysAlaHisAsnSerProArgAspPh 431

2392 ...................GGCAACCTTAGCCTCGTGGGCAATGCCC 2419
                        |||||||||::::::  ||||||
 431 eAlaSerArgThrLeuThrLeuGlyAsnLeuAsnValGluGlyAsnLeuT 448

2420 AAGCAACATTTAATCAAGCCACATTAAACGGCAACACATCGGCTTCGGGC 2469
        |||  :::  |||  ::::::||||||  |||      ::: 
 448 hrLeuThrGlySerValAlaAspIleLysGlyAsnLeuSerIleLeuAsn 464

2470 AATGCTTCATTT......AATCTAAGCGACCACGCCGTACAAAACGGCAG 2513
     :::|||:::|||      :::  |||::::::        :::|||:: 
 465 AspAlaThrPheLysGlyGluThrSerGluAsnLeuAsnIleThrGlyAs 481

2514 TCTGACGCTTTCCGGCAACGCTAAGGCAAACGTAAGCCATTCCGCACTCA 2563
     ::::|||  :::|||:::|||      |||:::::::::::::::::::| 
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 481 nPheThrAsnAsnGlyThrAlaAspIleAsnIleLysGlnGlyValValA 498

2564 ACGGTAATGTCTCCCTAGCCGATAAGGCAGTATTCCATTTTGAAAGCAGC 2613
     ||   :::  :::::::::::::|||:::  :::::::::  ::::::
 498 snIleGlnGlyAsnIleThrAsnLysGlyGlyLeuAsnIleThrThrAsn 514

2614 CGCTTTACCGGACAA.........ATCAGCGGC.............GG 2639
           ::::::|||         |||:::|||              || 
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2640 CAAGGATACGGCATTACACTTAAAAGACAGCGAATGGACGCTGCCGTCAG 2689
     |   |||      |||::::::|||||||||:::            ::::
 531 yGlyAsp......LeuAsnIleLysAspSerAsn............AsnA 542

2690 GCACGGAATTA.........GGCAATTTAAACCTTGACAACGCCACCATT 2730
     :::::|||:::         ||||||::::::      ::::::::::::
 542 snAlaGluIleGlnIleGlyGlyAsnIleSerGlnLysLysGlyAsnLeu 558

2731 ACACTCAATTCCGCCTATCGCCACGAT..................... 2757
     |||::::::|||           |||
 559 ThrIleSerSer............AspLysIleAsnIleThrLysLysIl 571

2758 .......GCGGCAGGGGCGCAAACCGGCAGTGCGACAGATGCGCCGCGCC 2800
             ||||||::::::  |||:::::::  :::::::|||
 571 eThrIleLysAlaGlyValAspGluGlyGlySerAspSerSerProAlaS 588

2801 GCCGTTCGCGCCGTTCGCGCCGTTCCCTATTATCCGTTACACCGCCAACT 2850
       ::::::
 588 erAsnAla..................................... 590

2851 TCGGTAGAATCCCGTTTCAACACGCTGACGGTAAACGGCAAATTGAACGG 2900
     ::::::      :::  :::||||||  ::::::|||  ||||||
 591 AsnLeuThrIleLysThrLysThrLeuGluLeuThrGlyAspLeuAsnIl 607

2901 TCAGGGAACATTCCGCTTTATGTCGGAACTCTTCGGCTACCGCAGCGACA 2950
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 607 eSerGlyPheAsnLys......AlaGluIleThrAlaLysAsnGlyAsnA 622

2951 AATTGAAGCTGGCGGAAAGTTCCGAAGGCACTTACACCTTGGCGGTCAAC 3000
       |||  :::::::::::::|||:::|||:::
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3001 AATACCGGCAACGAACCTGCAAGCCTCGAACAATTGACGGTAGTGGAAGG 3050
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 633 ..................AlaAsnAlaLysLysValThrPheAspLysVa 643

3051 AAAAGACAACAAACCGCTGTCCGAAAACCTTAATTTCACCCTGCAAAACG 3100
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 643 lLysAspSerLysIleSerAlaAsnGlyHisAsnValThr..... 656

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 656 ..................................................... 656

3151 GAGTTCCGCCTGCATAATCCGGTCAAAGAACAAGAGCTTTCCGACAAACT 3200
                                        |||:::::::|||::
 657 ................................LeuAsnSerLysVa 661

3201 CGGCAAGGCAGAAGCCAAAAAACAGGCGGAAAAAGACAACGCGCAAAGCC 3250
     :      :::::::::  ::::::|||:::  :::|||  ::::::
 661 lGluThrSerAsnSerAspSerSerAlaAspAspSerAsnAspAsnAsnT 678

3251 TTGACGCGCTGATTGCGGCCGGGCGCGATGCCGTCGAAAAGACAGAAAGC 3300
                |||:::|||
 678 hrGlyLeuThrIleSerAla.............................. 684

3301 GTTGCCGAACCGGCCCGGCAGGCAGGCGGGGAAAATGTCGGCATTATGCA 3350
                                        :::::::|||  :::  ::
 685 ............................LysAspValThrValAsnAs 691

3351 GGCGGAGGAAGAGAAAAAACGGGTGCAGGCGGATAAAGACACCGCCTTGG 3400
     :         :::  |||  ::::::  :::      |||:::  :
 691 nAspValThrSerHisLysThrIleAsnIleSerAlaThrThrGlyAsnV 708
```

```
3401 CGAAACAGCGCGAAGCGGAAACCCGGCCGGCTACCACCGCCTTCCCCCGC 3450
      ::     :::|||:::   |||      |||:::|||::: |||
 708 alThrThrLysGluSerThrThrIleAsnAlaAlaThrGly.SerValGl 724

3451 GCCCGCCGCGCCCGCCGGGATTTGCCGCAACTGCAACCCCAACCGCAGCC 3500
        :::|||   :::|||         :::          :::::::::
 724 uValThrAlaLysThrGlyAspIleSerGlyThrIleSerGlyAsnThrV 741

3501 CCAACCGCAGCGCGACCTGATCAGCCGTTATGCCAATAGCGGTTTGAGTG 3550
       |||   :::|||||||   |||   :::         :::
 741 alAsnValThrAlaThrAspSerLeuThrThrGlnAlaSer..... 754

3551 AATTTTCCGCCACGCTCAACAGCGTTTTCGCCGTACAGGACGAATTAGAC 3600
                   |||   :::   |||      :::|||:::   ||
 755 ............SerSerIleThrSerSerAsnGlyGlnThrThrLeuTh 767

3601 CGCGTATTTGCCGAAGACCGCCGCAACGCCGTTTGGACAAGCGGCATCCG 3650
     ||||        :::   |||::::::         :::|||||||:::
 767 rAlaLysAsnGlySerIleAlaGlySerIle......AspAlaAlaAsnV 782

3651 GGACACCAAACACT......ACCGTTCGCAAGATTTCCGCGCCTACCGCC 3694
       |||   ||||||      |||:::      :::::::::   :::
 782 alThrLeuAsnThrThrGlyThrLeuThrThrValAlaGlySerAsnIle 798

3695 AACAAACCGACCTGCGCCAAATCGGTATGCAGAAAAACCTCGGCAGCGGG 3744
     :::      :::   :::   ::::::      |||   :::
 799 LysAlaThrSerGlyThrLeuAlaIleAsnAlaLysAspAlaLysLeuAs 815

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 815 pGlyThrAlaSer..............GlyAspArgThrValValAsnA 827

3795 CGGCATCGGCAACTCGGCACGGCTTGCCCACGGCGCCGTTTTCGGGCAAT 3844
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3845 ACGGCATCGACAGGTTCTACATCGGCATCAGCGCGGGCGCGGGTTTTAGC 3894
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 844 ValAsnIleThrGlyAspLeuSerThrIleAsnGlyLeuAsnIleIleSe 860

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 860 rLysAsnGlyLysAsnThrVal......ValLeuLysGlyAlaGluIleA 875

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4027 GTCCAAAAAGCGGATTACCGCTACGAAAACGTCAATATCGCCACCCCCGG 4076
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 903 rAspGluGluArgGluThrLeuAlaLysLeuGlyValSerAlaValArgP 920

4077 CCTTGCATTCAACCGCTACCGCGCGGGCATTAAGGCAGATTATTCATTCA 4126
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 920 heValGluProAsnAsnThr...................IleThrVal 929

4127 AACCGGCGCAACACATTTCCATCACGC 4153
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ID   AAB01826 standard; Protein; 975 AA.
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AC   AAB01826;
XX
DT   11-SEP-2000  (first entry)
XX
DE   Haemophilus influenzae strain Joyc HMW2A protein, SEQ ID NO:30.
XX
KW   HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW   non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW   recombinant production; Escherichia coli; antibacterial; vaccine;
KW   human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW   detection; diagnosis.
XX
OS   Haemophilus influenzae strain Joyc.
XX
PN   WO200020609-A2.
XX
PD   13-APR-2000.
XX
PF   07-OCT-1999;   99WO-CA00938.
XX
PR   07-OCT-1998;   98US-0167568.
PR   08-DEC-1998;   98US-0206942.
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PA   (CONN-) CONNAUGHT LAB LTD.
XX
PI   Loosmore SM,  Yang Y,  Klein MH;
XX
DR   WPI; 2000-303789/26.
DR   N-PSDB; AAA52177.
XX
PT   Nucleic acid molecule for producing recombinant high molecular weight
PT   proteins of Haemophilus which are used as a vaccine to provide
PT   protection against Haemophilus induced diseases in humans -
XX
PS   Claim 12; Fig 19A-O; 307pp; English.
XX
CC   The invention relates to the recombinant production of Haemophilus
CC   influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC   expression construct used to effect recombinant expression comprises a
CC   promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC   to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC   influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC   clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC   hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC   and the hmwB and hmwC genes encode accessory proteins which are
CC   responsible for post-translational processing and secretion of the HMWA
CC   proteins. The modified hmwABC operon used in the expression construct of
CC   the invention contains an A gene modified such that it encodes only the
CC   mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC   and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC   strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC   vectors are used for the production of recombinant H. influenzae HMW
CC   proteins which can be used as vaccines to mediate a humoral or
CC   cell-mediated immune response to provide protection against diseases in
CC   humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC   pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC   antigens in immunoassays for detecting antibodies against Haemophilus,
CC   HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC   HMW proteins can be used to isolate and clone hmw genes from other
CC   non-typeable strains of Haemophilus via hybridisation reactions. The
CC   present sequence represents an HMWA protein from a non-typeable strain of
CC   H. influenzae.
XX
SQ   Sequence   975 AA;
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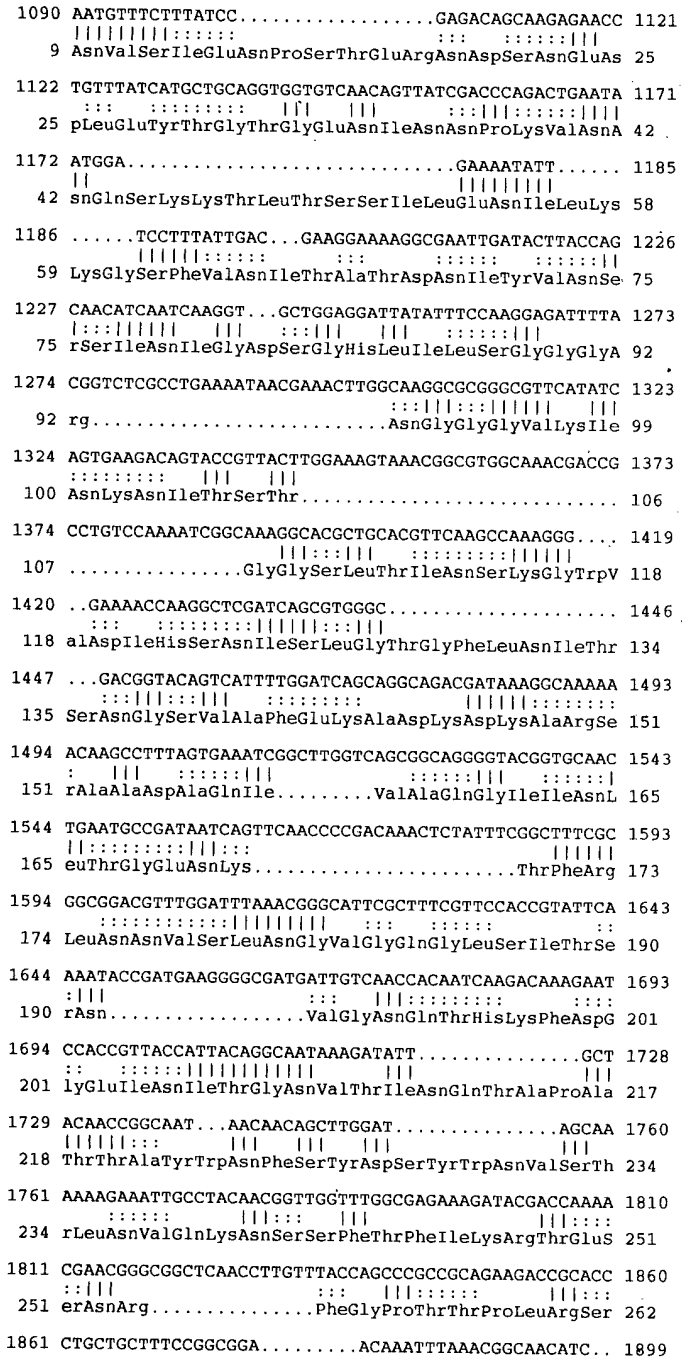
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59 LysGlySerPheValAsnIleThrAlaThrAspAsnIleTyrValAsnSe 75
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92 rg.....AsnGlyGlyGlyValLysIle 99
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100 AsnLysAsnIleThrSerThr..... 106
1374 CCTGTCCAAAATCGGCAAAGGCACGCTGCACGTTCAAGCCAAAGGG.... 1419
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1943 CGCACGCCTACAATCATTTAAACGACCATTGGTCGCAAAAAGAGGGCATT 1992
292 .....AsnGluAsnThrAsnAsnSerLysProLeu 301
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302 Pro.....LeuGlnPheAs 306
2043 AGCGGAAAACTTCCAAATTAAAGGCGGACAGGCGGTGGTTTCCCGCAATG 2092
306 nAlaAsnIleThrAlaIleGlyGlyGly..... 315
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316 .....SerValSerPheAspIleHis...AlaAsnHisSer..... 326
2143 TTTGGTGTCGCACCGCATCAAAGCCACACAATCTGTACACGTTCGGACTG 2192
327 ...GlyArgGlyAlaGluLeuLysMetAsnThrIleAsnIleSerAspGl 342
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 521 AlaGlnAsnAsnGlnLysThrIleIleAsnGlyAsnIleThrAsnGluGl 537

2640 CAAGGATACGGCATTACACTTAAAAGACAGCGAATGGACGCTGCCGTCAG 2689
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 537 yGlyAsp......LeuAsnIleLysAspSerAsn............AsnA 548

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 548 snAlaGluIleGlnIleGlyGlyAsnIleSerGlnLysLysGlyAsnLeu 564

2731 ACACTCAATTCCGCCTATCGCCACGAT..................... 2757
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 565 ThrIleSerSer............AspLysIleAsnIleThrLysLysIl 577

2758 .......GCGGCAGGGGCGCAAACCGGCAGTGCGACAGATGCGCCGCGCC 2800
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 577 eThrIleLysAlaGlyValAspGluGlyGlySerAspSerSerProAlaS 594

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 594 erAsnAla..................................... 596

2851 TCGGTAGAATCCCGTTTCAACACGCTGACGGTAAACGGCAAATTGAACGG 2900
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 649 lLysAspSerLysIleSerAlaAsnGlyHisAsnValThr.......... 662

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 662 .................................................. 662

3151 GAGTTCCGCCTGCATAATCCGGTCAAAGAACAAGAGCTTTCCGACAAACT 3200
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 663 ....................................LeuAsnSerLysVa 667

3201 CGGCAAGGCAGAAGCCAAAAAACAGGCGGAAAAAGACAACGCGCAAAGCC 3250
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3251 TTGACGCGCTGATTGCGGCCGGGCGCGATGCCGTCGAAAAGACAGAAAGC 3300
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 684 hrGlyLeuThrIleSerAla............................. 690

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 691 ............................LysAspValThrValAsnAs 697

3351 GGCGGAGGAAGAGAAAAAACGGGTGCAGGCGGATAAAGACACCGCCTTGG 3400
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     ::      :::|||:::   |||      |||:::|||::: |||
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3651 GGACACCAAACACT......ACCGTTCGCAAGATTTCCGCGCCTACCGCC 3694
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AC   AAW30294;
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DT   14-APR-1998  (first entry)
XX
DE   Non-typeable Haemophilus high mol.wt. surface protein HMW2.
XX
KW   Non-typeable Haemophilus; high molecular weight surface protein;
KW   HMW2; hmw2A gene; immunogen; vaccine; otitis media.
XX
OS   Haemophilus influenzae strain 12.
XX
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PD   09-OCT-1997.
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PF   01-APR-1997;   97WO-US04707.
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PR   01-APR-1996;   96US-0617697.
XX
PA   (BARE/) BARENKAMP S J.
XX
PI   Barenkamp SJ;
XX
DR   WPI; 1997-503038/46.
DR   N-PSDB; AAT90995.
XX
PT   High molecular weight proteins of non-typeable Haemophilus
PT   influenzae - useful for vaccine production
XX
PS   Claim 7; Page 73-78; 183pp; English.
XX
CC   This protein comprises the high molecular weight surface protein
CC   HMW2 (123 kDa) of non-typeable Haemophilus influenzae strain 12 that
CC   has the immunological ability to protect against disease caused by a
CC   non-typeable Haemophilus strain and is characterised by at least
CC   one surface-exposed B-cell epitope that is recognised by monoclonal
CC   antibody AD6.  The HMW2 amino acid sequence was deduced from the
CC   hmw2 gene sequence (see AAT90995 and AAT90997).  The expressed protein
CC   is truncated, starting at residue 442 of the full-length gene
CC   product.  HMW1 (see AAW30293), HMW3 (see AAW30291) and HMW4 (see
CC   AAW30292) have also been identified.  A conjugate comprising HMW2
CC   linked to an antigen, hapten or polysaccharide, and a synthetic
CC   peptide of 6-150 amino acids corresponding to at least protective
CC   epitope of HMW2 are also claimed.  HMW proteins, conjugates and
CC   peptides can be used in vaccines, as immunogens for preparation of
CC   antibodies and as antigens for detection of these antibodies.
XX
SQ   Sequence   1477 AA;


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     234 .............LeuAlaGlyGlnLysIleThrIleSerAspIleIleA 246

     265 ..CCGATGATTGATTTTTCTGTGGTGTCGCGTAACGGCGTGGCGGCATTG 312
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     246 snProThrIleThrTyrSerIleAlaAlaProGluAsnGluAlaValAsn 262

     313 GTGGGCGATCAATATATTGTGAGCGTGGCACATAACGGCGGCTATAACAA 362
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     263 LeuGlyAsp..............IlePheAlaLysGlyGlyAsnIleAs 274

     363 CGTT.........................GATTTTGGTGCGGAAGGAA 385
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     308 AlaGluIleGlyGlyValIleSerAlaGlnAsnGlnGlnAlaLysGlyGl 324

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     341 leAspLeuSerGlyLysGluGlyGlyGluThrTyrLeuGlyGlyAspGlu 357

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     358 Arg.................GlyGluGlyLysAsnGlyIleGlnLeuAl 368

     621 TGAAGATGAGCCCAATAACCGCGAAAGTTCATATCATATTGCAAGT.... 666
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     667 .............GCGTATTCTTGG............CTCGTTGGTGGC 690
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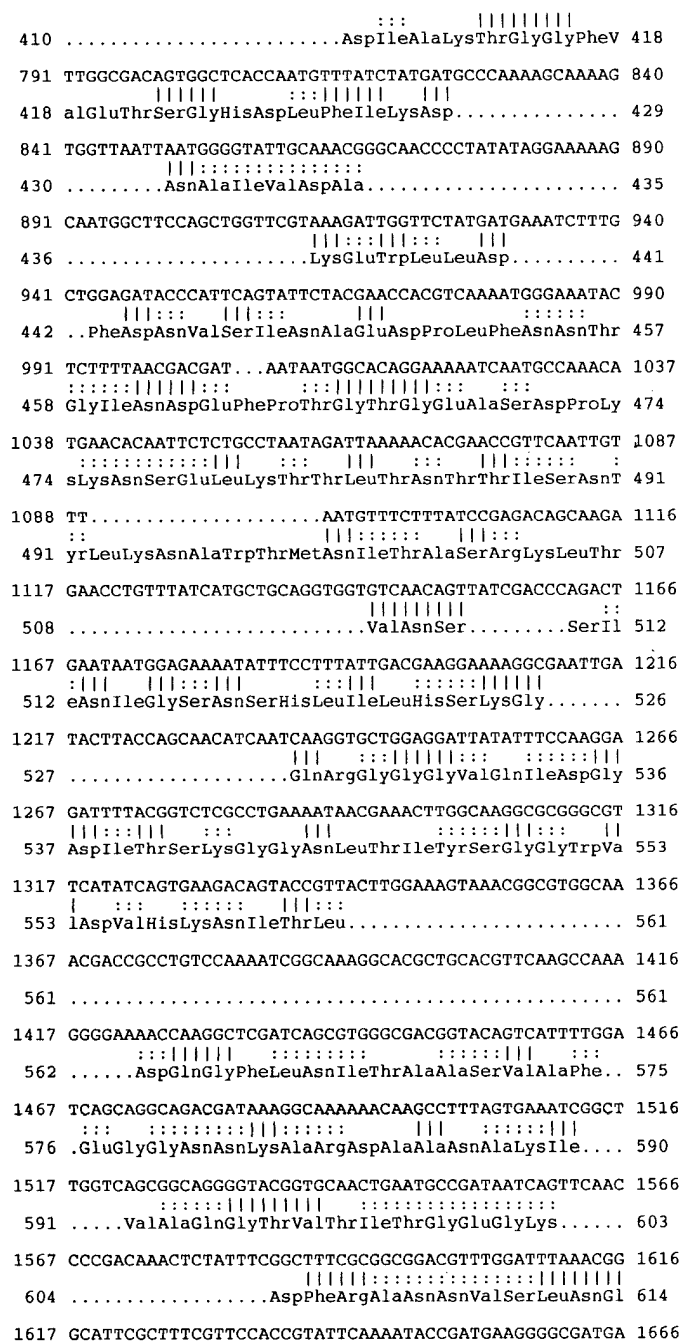
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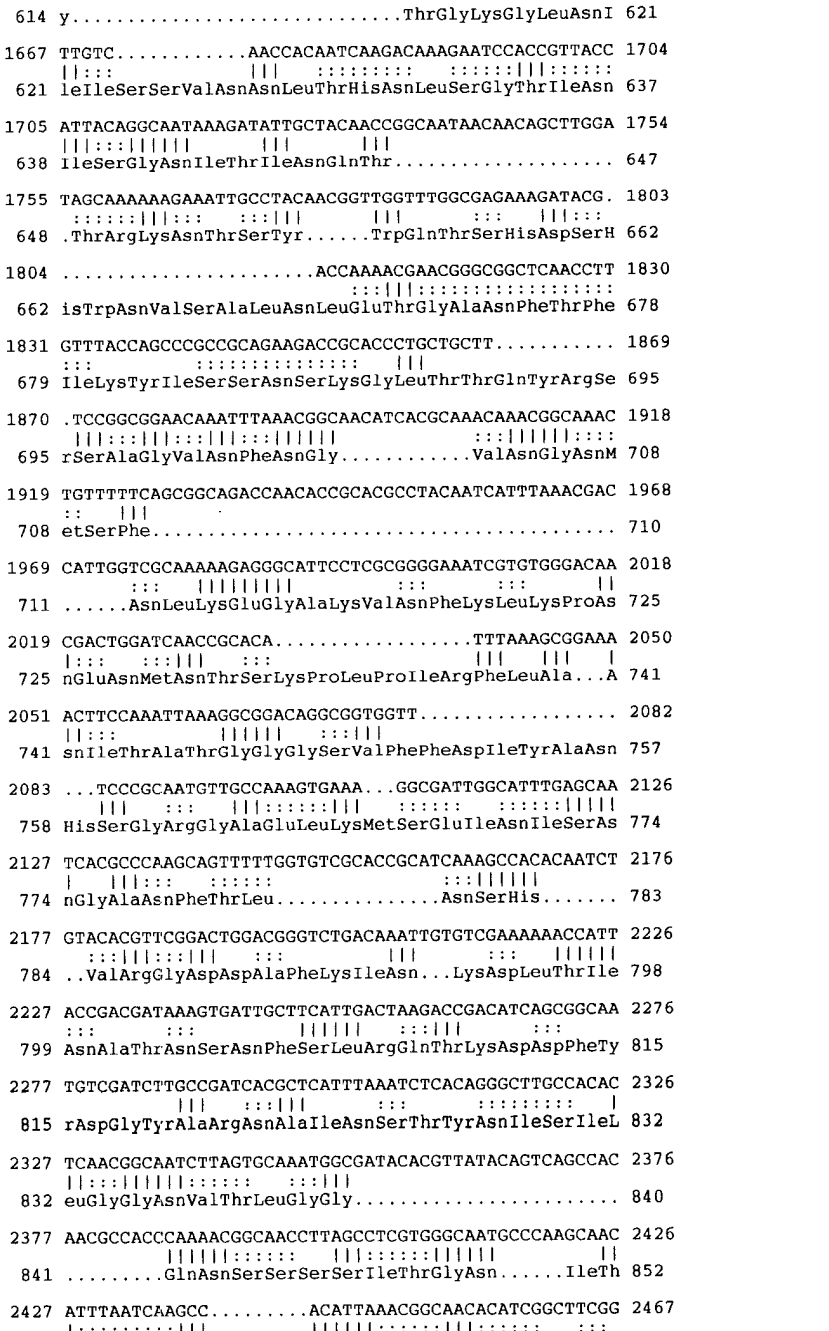
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seq_documentation_block:
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AC   AAR63505;
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DT   25-JUN-1995  (first entry)
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DE   Haemophilus high molecular weight protein HMW1.
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KW   High molecular weight protein; HMW1; protective vaccine; otitis;
KW   sinusitis; bronchitis; Hib.
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OS   Haemophilus.
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PN   WO9421290-A.
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PD   29-SEP-1994.
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PF   15-MAR-1994;   94WO-US02550.
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PR   16-MAR-1993;   93US-0038682.
XX
PA   (BARE/) BARENKAMP S J.
PA   (SGEM/) ST GEME J W.
XX
PI   Barenkamp SJ,  St GEME JW;
XX
DR   WPI; 1994-316665/39.
DR   Q-PSDB; Q72293.
XX
PT   New immunogenic high mol. wt. proteins of non typeable
PT   Haemophilus - useful in protective vaccines
XX
PS    Claim 2; Page 31; 127pp; English.
XX
CC   The HMW1 protein encoded by this sequence is useful in a vaccine to
CC   protect against disease caused by non-typeable Haemophilus which are
CC   not controlled by H. influenzae type b (Hib) vaccines.  The encoded
CC   protein can also be used as a carrier for protective Hib
CC   polysaccharide (in a conjugate vaccin against meningitis) or for
CC   other antigens, haptens, etc.
XX
SQ   Sequence   1536 AA;
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1776 CAACGGT...TGGTTTGGCGAGAAAGATACGACCAAAACGAACGGGCGGC 1822
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 933 sGlyGlyAlaArgPheLysAspIleAspAsnSerLys.........AsnL 947

1823 TCAACCTTGTTTACCAGCCCGCCGCAGAAGACCGCACCCTGCTGCTTTCC 1872
     ||:::::::::   :::   ::::::      ||||||::::::   :::
 947 euSerIleThrThrAsnSerSerSerThrTyrArgThrIleIleSerGly 963

1873 GGCGGAACAAATTTAAACGGCAACATCACGCAAACAAACGGCAAACTGTT 1922
     :::   ||||||   ||||||:::::::::   ||||||
 964 AsnIleThrAsnLysAsnGlyAspLeuAsnIleThrAsn........... 976

1923 TTTCAGCGGCAGACCAACACCGCACGCCTACAATCATTTAAACGACCATT 1972
       :::|||      |||                 :::::::::
 977 ....GluGlySerAspThrGlu.........MetGlnIleGlyGlyAspV 989

1973 GGTCGCAAAAAGAGGGCATTCCTCGCGGGGAAATCGTGTGGGACAACGAC 2022
       ||||||||||||            |||::::::::::   ::::::|||
 989 alSerGlnLysGlu.............GlyAsnLeuThrIleSerSerAsp 1001

2023 TGGATCAACCGCACATTTAAAGCGGAAAACTTCCAAATTAAAGGCGGACA 2072
       ||||||   |||        :::::::::   ||||||:::|||
1002 LysIleAsnIleThr.........LysGlnIleThrIleLysAlaGly.. 1014

2073 GGCGGTGGTTTCCCGCAATGTTGCCAAAGTGAAAGGCGATTGGCATTTGA 2122
                        |||         ::::::|||         :
1015 ...................ValAspGlyGluAsnSerAspSerAspAlaT 1025

2123 GCAATCACGCCCAAGCAGTTTTTGGTGTCGCACCGCATCAAAGCCACACA 2172
     ::|||:::|||:::                                  |||
1025 hrAsnAsnAlaAsnLeu.............................Thr 1031

2173 ATCTGTACACGTTCGGACTGGACGGGTCTGACAAATTGTGTCGAAAAAAC 2222
     |||   |||:::                                   |||
1032 IleLysThrLys.............................GluLeuLy 1038

2223 CATTACCGACGATAAAGTGATTGCTTCATTGACTAAGACCGACATCAGCG 2272
       :::|||:::|||      |||:::::::::::::|||:::::|||::::
1038 sLeuThrGlnAspLeuAsnIleSerGlyPheAsnLysAlaGluIleThrA 1055

2273 GCAATGTCGATCTTGCCGATCACGCTCATTTAAATCTCACAGGGCTTGCC 2322
     :::::   |||   :::|||
1055 laLys...AspGlySerAsp.........................Leu 1061

2323 ACACTCAACGGCAATCTTAGTGCAAATGGCGATACACGTTATACAGTCAG 2372
     |||::::::::::::   ||||||:::|||   :::          |||::
1062 ThrIleGlyAsnThrAsnSerAlaAspGlyThrAsnAlaLysLysValTh 1078

2373 CCACAACGCCACCCAAAACGGCAACCTTAGCCTCGTGGGCAATGCCCAAG 2422
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1078 rPheAsnGlnValLysAspSerLysIleSerAlaAspGly.......... 1091

2423 CAACATTTAATCAAGCCACATTAAACGGCAACACATCGGCTTCGGGCAAT 2472
            :::::::::||||||:::::::::::::::::::||||||:::
1092 ........HisLysValThrLeuHisSerLysValGluThrSerGlySer 1105

2473 GCTTCATTTAATCTAAGCGACCACGCCGTACAAAACGGCAGTCTGACGCT 2522
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2523 TTCCGGCAACGCTAAGGCAAACGTAAGCCATTCCGCACTCAACGGTAATG 2572
     :      :::||||||   ||||||:::          :::|||:::|||:
1121 e......AspAlaLys...AsnValThr.........ValAsnAsnAsnI 1132

2573 TCTCCCTAGCCGATAAGGCAGTATTCCATTTTGAAAGCAGCCGCTTTACC 2622
     :::::   :::   |||||||||          :::   |||      :::
1132 leThr...SerHisLysAlaVal.........SerIleSerAlaThrSer 1144

2623 GGACAAATCAGCGGCGGCAAGGATACGGCATTACACTTAAAA......GA 2666
     |||:::|||:::            |||:::::::::             ::
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2667 CAGCGAATGGACGCTGCCGTCAGGCACGGAATTAGGCAATTTAAACCTTG 2716
     :   |||   |||       :::|||:::   ||||||:::::::::   :
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     ::::::::::::::|||||:::::::::            |||::::::
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1195 AsnIleSerGlyAsnThrValThrValThrAlaAsnSerGlyAlaLeuTh 1211
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2817 GCGCCGTTCCCTATTATCCGTTACACCGCCAACTTCGGTAGAATCCCGTT 2866
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2867 TCAACACGCTGACGGTAAACGGCAAATTGAACGGTCAGGGAACA..... 2910
1228 erGlnSerGlyAspIleGlyGlyThrIleSerGly...GlyThrValGlu 1243

2911 TTCCGCTTTATGTCGGAACTCTTCGGCTACCGCAGCGACAAATTGAAGCT 2960
1244 ValLysAlaThrGluSerLeuThrThrGlnSerAsnSerLysIleLys.. 1259

2961 GGCGGAAAGTTCCGAAGGCACTTACACCTTGGCGGTC..... 2997
1260 .AlaThrThrGlyGluAlaAsnValThrSerAlaThrGlyThrIleGlyG 1276

2998 ..........AACAATACCGGCAACGAACCTGCAAGCCTCGAACAATTG 3036
1276 lyThrIleSerGlyAsnThrValAsnValThrAlaAsnAlaGlyAspLeu 1292

3037 ACGGTA.....................GTGGAAGGAAAAGACAACAA 3062
1293 ThrValGlyAsnGlyAlaGluIleAsnAlaThrGluGlyAlaAlaThrLe 1309

3063 ACCGCTGTCCGAAAACCTTAATTTCACCCTGCAAAACGAACACGTCGATG 3112
1309 uThrThrSerSerGlyLysLeuThrThrGluAlaSerSerHisIleThrS 1326

3113 CCGGCGCGTGGCGTTACCAACTCATCCGCAAAGACGGCGAGTTCCGCCTG 3162
1326 er.AlaLysGlyGlnValAsnLeuSerAlaGlnAspGlySerValAlaGl 1342

3163 CATAATCCGGTCAAAGAACAAGAGCTTTCCGACAAACTCGGCAAGGCAGA 3212
1342 ySerIleAsnAlaAlaAsnValThrLeuAsnThrThrGlyThrLeuThrT 1359

3213 AGCCAAAAAACAGGCGGAAAAAGACAACGCGCAAAGCCTTG 3253
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seq_documentation_block:

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ID   AAB01846 standard; Protein; 1536 AA.
XX
AC   AAB01846;
XX
DT   11-SEP-2000  (first entry)
XX
DE   Haemophilus influenzae strain 12 HMW1A protein, SEQ ID NO:67.
XX
KW   HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW   non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW   recombinant production; Escherichia coli; antibacterial; vaccine;
KW   human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW   detection; diagnosis.
XX
OS   Haemophilus influenzae strain 12.
XX
PN   WO200020609-A2.
XX
PD   13-APR-2000.
XX
PF   07-OCT-1999;   99WO-CA00938.
XX
PR   07-OCT-1998;   98US-0167568.
PR   08-DEC-1998;   98US-0206942.
XX
PA   (CONN-) CONNAUGHT LAB LTD.
XX
PI   Loosmore SM,  Yang Y,  Klein MH;
XX
DR   WPI; 2000-303789/26.
DR   N-PSDB; AAA52195.
XX
PT   Nucleic acid molecule for producing recombinant high molecular weight
PT   proteins of Haemophilus which are used as a vaccine to provide
PT   protection against Haemophilus induced diseases in humans -
XX
PS   Example 16; Fig 28A-Q; 307pp; English.
XX
CC   The invention relates to the recombinant production of Haemophilus
CC   influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC   expression construct used to effect recombinant expression comprises a
CC   promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC   to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC   influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC   clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC   hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC   and the hmwB and hmwC genes encode accessory proteins which are
CC   responsible for post-translational processing and secretion of the HMWA
CC   proteins. The modified hmwABC operon used in the expression construct of
CC   the invention contains an A gene modified such that it encodes only the
CC   mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC   and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC   strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC   vectors are used for the production of recombinant H. influenzae HMW
CC   proteins which can be used as vaccines to mediate a humoral or
CC   cell-mediated immune response to provide protection against diseases in
CC   humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC   pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC   antigens in immunoassays for detecting antibodies against Haemophilus,
CC   HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC   HMW proteins can be used to isolate and clone hmw genes from other
CC   non-typeable strains of Haemophilus via hybridisation reactions. The
CC   present sequence represents an HMWA protein from a non-typeable strain of
CC   H. influenzae.
XX
SQ   Sequence   1536 AA;
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             Ratio:  0.460                Gaps:     60
 Percent Similarity:  51.015   Percent Identity: 20.981

alignment_block:
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  349 GlyGluThrTyrLeuGly.........................GlyAs 356

  177 AAATAAAGGCAAGTTTGCAGTCGGGGCGAAAGATATTGAGGTTTACAACA 226
  356 pGluArgGlyGlu.........GlyLysLysGlyIleGlnLeuAlaLysL 370

  227 AAAAAGGGGAGTTGGTCGGCAAATCAATGACAAAAGCCCCGATGATTGAT 276
  370 ys..................ThrSerLeuGluLysGlySerThrIleAsn 380

  277 TTTTCTGTGGTGTCGCGTAACGGCGTGGCGGCATTGGTGGGCGATCAATA 326
  381 ValSerGlyLysGluLysGlyGlyArgAlaIleValTrpGlyAspIleAl 397

  327 TATTGTG.............................AGCGTGGCACATA 346
  397 aLeuIleAspGlyAsnIleAsnAlaGlnGlySerGlyAspIleAlaLysT 414

  347 ACGGCGGCTAT..................................... 357
  414 hrGlyGlyPheValGluThrSerGlyHisAspLeuPheIleLysAspAsn 430

  358 .................................AACAACGTTGATTT 371
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                                                  :::||||||:::::
431 AlaIleValAspAlaLysGluTrpLeuLeuAspProAspAsnValSerIl 447

372 TGGTGCGGAA......GGAAGAAATCCCGATCAACATCGTTTTACTTAT. 414
    ::::||||||      ||||||:::      ::::::          |||
447 eAsnAlaGluThrAlaGlyArgSerAsnThrSerGluAspAspGluTyrT 464

415 ...................AAAATTGTGAAACGGAATAATTATAAAGCA 444
                        :::      ||||||||||:::   |||:::
464 hrGlySerGlyAsnSerAlaSerThrProLysArgAsnLysGluLysThr 480

445 GGGACTAAAGGCCATCCTTATGGCGGCGATTATCATATGCCGCGTTTGCA 494
      |||           :::   :::|||:::           :::   :
481 .ThrLeuThrAsnThrThrLeuGluSerIleLeuLysLysGlyThrPheV 497

495 TAAATTTGTCACAGATGCAGAACCTGTTGAAATGACCAGTTATATGGATG 544
    ::|||::::::     |||:::                  |||::::::
497 alAsnIleThrAlaAsnGlnArg...................IleTyrVal 507

545 GGCGGAAATATATCGATCAAAATAATTACCCTGACCGTGTTCGTATTGGG 594
    ::::::::::|||::::::::      :::||||||::::::      ||
508 AsnSerSerIleAsnLeuSerAsnGlySerLeuThrLeuTrpSerGluGl 524

595 GCAGGCAGGC..........................AATATTGGCGATC 617
    |:::::::|||                        :::   ||||||
524 yArgSerGlyGlyGlyValGluIleAsnAsnAspIleThrThrGlyAspA 541

618 TGATGAAGATGAGCCCAATAACC..................GCGAAAGTT 649
        :::   :::   :::|||                  :::   |||
541 spThrArgGlyAlaAsnLeuThrIleTyrSerGlyGlyTrpValAspVal 557

650 CATATCATATTGCAAGTGCGTATTCTTGGCTCGTTGGTGGCAATACCTTT 699
    |||      :::::::::          |||::::::  :::   |||
558 HisLysAsnIleSerLeuGlyAlaGlnGlyAsnIle..AsnIleThrAla 573

700 GCACAAAAT..............GGATCA..............GGTGG 719
      |||:::              ||||||              |||
574 LysGlnAspIleAlaPheGluLysGlySerAsnGlnValIleThrGlyGl 590

720 TGGCACAGTCAACTTAGGTAGTGAAAAAATTAAACATAGCCCATATGGTT 769
     ||||||::::::   |||:::::|||                 ||||
590 nGlyThrIleThrSerGlyAsnGlnLys.................GlyP 601

770 TTTTACCAACAGGAGGCTCATTTGGCGACAGTGGCTCACCAATGTTTATC 819
    ||     ::::::   |||:::::::   :::||||||   :::   :::
601 heArgPheAsnAsnValSerLeuAsnGlyThrGlySerGlyLeuGlnPhe 617

820 TATGATGCCCAAAAGCAAAAGTGGTTAATTAATGGGGTATTGCAAACGGG 869
              :::   :::|||:::  |||::::::   ::::::
618 ThrThrLysArgThrAsnLysTyrAlaIleThrAsnLysPheGluGlyTh 634

870 CAACCCCTATATAGGAAAAAGCAAT...GGCTTCCAGCTGGTTCGTAAAG 916
                  ||||||   |||   ::::::   |||   :::::::
634 rLeuAsnIleSerGlyLysValAsnIleSerMetValLeuProLysAsnG 651

917 ATTGGTTCTATGATGAAATCTTTGCTGGAGATACCCAT......TCAGTA 960
    ::      |||||||:::   |||   |||   |||:::        :::
651 luSerGlyTyrAspLys...PheLysGlyArgThrTyrTrpAsnLeuThr 666

961 TTCTACGAACCACGTCAAAATGGGAAATACTCTTTTAACGACGATAATAA 1010
        :::      :::::::|||:::::::::::::::   |||:::::
667 SerLeuAsnValSerGluSerGlyGluPheAsnLeuThrIleAspSerAr 683

1011 TGGCACA.........GGAAAAATCAATGCCAAACATGAACACAATTCTC 1051
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683 gGlySerAspSerAlaGlyThrLeuThrGlnProTyrAsnLeuAsnGlyI 700

1052 TGCCT...AATAGATTAAAAACACGAACCGTTCAATTGTTTAATGTTTCT 1098
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1099 TTATCCGAGACAGCAAGAGAACCTGTTTATCATGCTGCAGGTGGTGTCAA 1148
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716 ValAsnPheAspIleLysAlaProIle.............GlyIleAs 727

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727 nLysTyr.....................SerSerLeuAsnTyrAlaSer. 736

1199 AAGGAAAAGGCGAATTGATACTTACCAGCAACATCAATCAAGGTGCTGGA 1248
                          :::::::::|||||||:::   :::::::|||
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     |||          :::   ||||||||||:::      ::::::::::::::
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     :   |||      ||||||                      ::::::|||
760 l...GlnThrProGlyValValIleAsnSerLysTyrPheAsnValSerT 776

1328 AAGACAGTACCGTTACTTGGAAAGTAAACGGC..................... 1359
          |||:::::::   :::|||::::::|||
776 hrGlySerSerLeuArgPheLysThrSerGlySerThrLysThrGlyPhe 792

1360 ...GTGGCAAACGAC...CGCCTGTCCAAAATCGGCAAAGGCACGCTGCA 1403
        :::   :::|||      |||:::      |||   :::
793 SerIleGluLysAspLeuThrLeuAsnAlaThrGlyGlyAsnIleThrLe 809

1404 CGTTCAAGCCAAAGGGGAAAAC..........................C 1426
      :::|||::::::|||   :::                          :
809 uLeuGlnValGluGlyThrAspGlyMetIleGlyLysGlyIleValAlaL 826

1427 AAGGCTCGATCAGCGTGGGCGACGGTACAGTCATTTTGGATCAGCAGGCA 1476
     ::   :::|||:::          |||::::::   :::
826 ysLysAsnIleThrPheGluGlyGlyAsnIleThrPhe............ 838

1477 GACGATAAAGGCAAAAAACAAGCCTTTAGTGAAATCGGCTTGGTCAGCGG 1526
               |||::::::::::|||   :::||||||          :::||
839 .........GlySerArgLysAlaValThrGluIle.........GluGl 849

1527 CAGGGGTACGGTGCAACTGAATGCCGATAATCAGTTCAACCCCGACAAAC 1576
     |:::   |||::::::   ||||||:::
849 yAsnValThrIleAsnAsnAsnAlaAsn..................... 858

1577 TCTATTTCGGCTTTCGCGGCGGACGTTTGGATTTAAACGGGCATTCGCTT 1626
                                  :::   |||   |||   ::::::
859 .........................ValThrLeuIleGlySerAspPhe 866

1627 TCGTTCCACCGTATTCAAAATACCGATGAAGGGGCGATGATTGTCAACCA 1676
     :::   |||:::          |||   :::       :::|||:::|||
867 AspAsnHisGlnLysProLeuThrIleLysLysAspValIleIleAsnSe 883

1677 CAATCAA......GACAAAGAATCCACCGTTACCATTACAGGCAATAAAG 1720
      ::::::                :::   |||:::|||:::||||||
883 rGlyAsnLeuThrAlaGlyGlyAsnIleValAsnIleAlaGlyAsnLeuT 900

1721 ATATTGCTACAACCGGCAAT.............................. 1740
       :::   ::::::::::|||
900 hrValGluSerAsnAlaAsnPheLysAlaIleThrAsnPheThrPheAsn 916

1741 ..............AACAACAGCTTGGATAGCAAAAAAGAAATTGCCTA 1775
                    :::|||:::   :::|||:::   :::||||||
917 ValGlyGlyLeuPheAspAsnLysGlyAsnSerAsnIleSerIleAlaLy 933

1776 CAACGGT...TGGTTTGGCGAGAAAGATACGACCAAAACGAACGGGCGGC 1822
     :::|||      |||   :::   |||:::::::|||          :::|
933 sGlyGlyAlaArgPheLysAspIleAspAsnSerLys.........AsnL 947

1823 TCAACCTTGTTTACCAGCCCGCCGCAGAAGACCGCACCCTGCTGCTTTCC 1872
     ||::::::::::   :::   ::::::      ||||||::::::   :::
947 euSerIleThrThrAsnSerSerSerThrTyrArgThrIleIleSerGly 963

1873 GGCGGAACAAATTTAAACGGCAACATCACGCAAACAAACGGCAAACTGTT 1922
     :::   ||||||   ||||||::::::::::   ||||||
964 AsnIleThrAsnLysAsnGlyAspLeuAsnIleThrAsn.......... 976
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989 alSerGlnLysGlu............GlyAsnLeuThrIleSerSerAsp 1001

2023 TGGATCAACCGCACATTTAAAGCGGAAAACTTCCAAATTAAAGGCGGACA 2072
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2073 GGCGGTGGTTTCCCGCAATGTTGCCAAAGTGAAAGGCGATTGGCATTTGA 2122
1015 ..................ValAspGlyGluAsnSerAspSerAspAlaT 1025

2123 GCAATCACGCCCAAGCAGTTTTTGGTGTCGCACCGCATCAAAGCCACACA 2172
1025 hrAsnAsnAlaAsnLeu.............................Thr 1031

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2223 CATTACCGACGATAAAGTGATTGCTTCATTGACTAAGACCGACATCAGCG 2272
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2373 CCACAACGCCACCCAAAACGGCAACCTTAGCCTCGTGGGCAATGCCCAAG 2422
1078 rPheAsnGlnValLysAspSerLysIleSerAlaAspGly..... 1091

2423 CAACATTTAATCAAGCCACATTAAACGGCAACACATCGGCTTCGGGCAAT 2472
1092 ........HisLysValThrLeuHisSerLysValGluThrSerGlySer 1105

2473 GCTTCATTTAATCTAAGCGACCACGCCGTACAAAACGGCAGTCTGACGCT 2522
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1121 e......AspAlaLys...AsnValThr.........ValAsnAsnAsnI 1132

2573 TCTCCCTAGCCGATAAGGCAGTATTCCATTTTGAAAGCAGCCGCTTTACC 2622
1132 leThr...SerHisLysAlaVal.........SerIleSerAlaThrSer 1144

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2667 CAGCGAATGGACGCTGCCGTCAGGCACGGAATTAGGCAATTTAAACCTTG 2716
1161 nValGluIleThrAlaGlnThrGlySerIleLeuGlyGlyIleGluSerS 1178

2717 ACAACGCCACCATTACACTCAATTCCGCCTATCGCCACGATGCGGCAGGG 2766
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1260 .AlaThrThrGlyGluAlaAsnValThrSerAlaThrGlyThrIleGlyG 1276

2998 ..........AACAATACCGGCAACGAACCTGCAAGCCTCGAACAATTG 3036
1276 lyThrIleSerGlyAsnThrValAsnValThrAlaAsnAlaGlyAspLeu 1292

3037 ACGGTA.....................GTGGAAGGAAAAGACAACAA 3062
1293 ThrValGlyAsnGlyAlaGluIleAsnAlaThrGluGlyAlaAlaThrLe 1309

3063 ACCGCTGTCCGAAAACCTTAATTTCACCCTGCAAAACGAACACGTCGATG 3112
1309 uThrThrSerSerGlyLysLeuThrThrGluAlaSerSerHisIleThrS 1326

3113 CCGGCGCGTGGCGTTACCAACTCATCCGCAAAGACGGCGAGTTCCGCCTG 3162
1326 er.AlaLysGlyGlnValAsnLeuSerAlaGlnAspGlySerValAlaGl 1342

3163 CATAATCCGGTCAAAGAACAAGAGCTTTCCGACAAACTCGGCAAGGCAGA 3212
1342 ySerIleAsnAlaAlaAsnValThrLeuAsnThrThrGlyThrLeuThrT 1359

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1359 hrValLysGlySerAsnIleAsnAlaThrSerGlyThrLeu 1372
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XX
DT 11-SEP-2000 (first entry)
XX
DE Haemophilus influenzae strain PMH1 mature HMW2A protein, SEQ ID NO:57.
XX
KW Mature HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW recombinant production; Escherichia coli; antibacterial; vaccine;
KW human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW detection; diagnosis.
XX
OS Haemophilus influenzae strain PMH1.
XX
PN WO200020609-A2.
XX
PD 13-APR-2000.
XX
PF 07-OCT-1999; 99WO-CA00938.
XX
PR 07-OCT-1998; 98US-0167568.
PR 08-DEC-1998; 98US-0206942.
XX
PA (CONN-) CONNAUGHT LAB LTD.
XX
PI Loosmore SM, Yang Y, Klein MH;
XX
DR WPI; 2000-303789/26.

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DR   N-PSDB; AAA52190.
XX
PT   Nucleic acid molecule for producing recombinant high molecular weight
PT   proteins of Haemophilus which are used as a vaccine to provide
PT   protection against Haemophilus induced diseases in humans -
XX
PS   Claim 8; Fig 25A-O; 307pp; English.
XX
CC   The invention relates to the recombinant production of Haemophilus
CC   influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC   expression construct used to effect recombinant expression comprises a
CC   promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC   to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC   influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC   clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC   hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC   and the hmwB and hmwC genes encode accessory proteins which are
CC   responsible for post-translational processing and secretion of the HMWA
CC   proteins. The modified hmwABC operon used in the expression construct of
CC   the invention contains an A gene modified such that it encodes only the
CC   mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC   and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC   strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC   vectors are used for the production of recombinant H. influenzae HMW
CC   proteins which can be used as vaccines to mediate a humoral or
CC   cell-mediated immune response to provide protection against diseases in
CC   humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC   pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC   antigens in immunoassays for detecting antibodies against Haemophilus,
CC   HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC   HMW proteins can be used to isolate and clone hmw genes from other
CC   non-typeable strains of Haemophilus via hybridisation reactions. The
CC   present sequence represents a mature HMWA protein from a non-typeable
CC   strain of H. influenzae.
XX
SQ   Sequence   1004 AA;


alignment_scores:
            Quality:  274.00              Length:   1077
              Ratio:  0.531                Gaps:     49
 Percent Similarity:  47.911   Percent Identity: 20.149

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     821 ATGATGCCCAAAAGCAAAAGTGGTTAATTAATGGGGTATTGCAAACGGGC 870
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     871 AACCCCTATATAGGAAAAAGCAATGGCTTCCAGCTGGTTCGTAAAGATTG 920

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     281 AsnIleAlaGlnGlySerThr.........AlaAsnPheHisIle...Ly 293

    1329 AGACAGTACCGTTACTTGGAAAGTAAAC.........GGCGTGGCAAACG 1369
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     293 sThrSerValMetThrProLysProAsnSerAsnTyrAlaLeuPheAsnG 310

    1370 ACCGCCTGTCCAAAATCGGCAAAGGCACGCTGCACGTTCAAGCCAAAGGG 1419
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494 snGlyThrSerIleIleAspIleThrGlnGlyValValAsnLeu..... 508
1837 CAGCCCGCCGCAGAAGACCGCACCCTGCTGCTTTCCGGCGGAACAAATTT 1886
508 508
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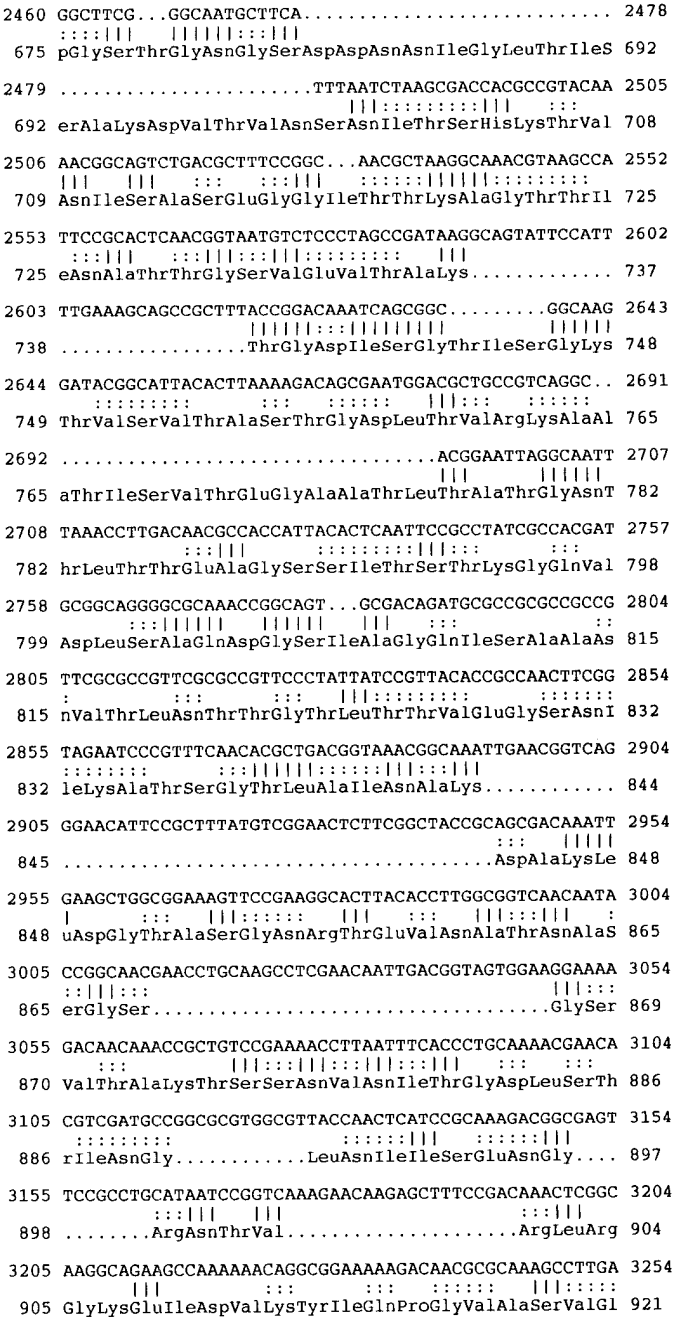
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2758 GCGGCAGGGGCGCAAACCGGCAGT...GCGACAGATGCGCCGCGCCGCCG 2804
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DT   11-SEP-2000  (first entry)
XX
DE   Haemophilus influenzae strain PMH1 HMW2A protein, SEQ ID NO:55.
XX
KW   HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW   non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW   recombinant production; Escherichia coli; antibacterial; vaccine;
KW   human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW   detection; diagnosis.
XX
OS   Haemophilus influenzae strain PMH1.
XX
PN   WO200020609-A2.
XX
PD   13-APR-2000.
XX
PF   07-OCT-1999;   99WO-CA00938.
XX
PR   07-OCT-1998;   98US-0167568.
PR   08-DEC-1998;   98US-0206942.
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PA   (CONN-) CONNAUGHT LAB LTD.
XX
PI   Loosmore SM,  Yang Y,  Klein MH;
XX
DR   WPI; 2000-303789/26.
DR   N-PSDB; AAA52189.
XX
PT   Nucleic acid molecule for producing recombinant high molecular weight
PT   proteins of Haemophilus which are used as a vaccine to provide
PT   protection against Haemophilus induced diseases in humans -
XX
PS   Claim 12; Fig 25A-O; 307pp; English.
XX
CC   The invention relates to the recombinant production of Haemophilus
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CC   expression construct used to effect recombinant expression comprises a
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CC   HMW proteins can be used to isolate and clone hmw genes from other
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CC   present sequence represents an HMWA protein from a non-typeable strain of
CC   H. influenzae.
XX
SQ   Sequence   1010 AA;


alignment_scores:
           Quality:  274.00              Length:   1077
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 Percent Similarity:  47.911   Percent Identity: 20.149

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  911 GlyLysGluIleAspValLysTyrIleGlnProGlyValAlaSerValGl 927

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      :   :::|||   |||   |||   ::::::||||||:::::::::::::
  927 uGluValIleGluAlaLysArg...ValLeuGluLysValLysAspLeuS 943

 3305 CCGAACCGGCCCGGCAGGCAGGCGGGGAAAATGTCGGCATTATGCAGGCG 3354
      :::::      |||::::::   ::::::   :::|||:::      :::
  943 erAspGluGluArgGluThrLeuAlaLys...LeuGlyValSerAlaVal 958

 3355 GAGGAAGAGAAAAAACGGGTGCAGGCGGATAAAGACACCGCCTTGGCGAA 3404
                 :::   |||:::   ::::::      ::::::
  959 ............ArgPheValGluProAsnAsnAlaIleThrIleAsnTh 971

 3405 ACAGCGCGAAGCGGAAACCCGGCCGGCTACC 3435
       |||:::|||      |||||||||::::::
  971 rGlnAsnGluPheThrThrArgProSerSer 981

seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1993.DAT:AAR41723

seq_documentation_block:
ID   AAR41723 standard; Protein; 1536 AA.
XX
AC   AAR41723;
XX
DT   26-APR-1994  (first entry)
XX
DE   High molecular weight protein 1 (HMW1).
XX
KW   HMW; high molecular weight protein; virus; vaccine; influenza;
KW   epitope; immunity; haemophilus influenzae.
XX
OS   Haemophilus influenzae.
XX
PN   WO9319090-A.
XX
PD   30-SEP-1993.
XX
PF   16-MAR-1993;   93WO-US02166.
XX
PR   16-MAR-1992;   92GB-0005704.
XX
PA   (BARE/) BARENKAMP S J.
PA   (INRM ) INSERM INST NAT SANTE & RECH MEDICALE.
XX
PI   Barenkamp SJ;
XX
DR   WPI; 1993-320683/40.
DR   N-PSDB; AAQ49506.
XX
PT   High molecular weight surface proteins - of non-typeable
PT   haemophilus which exhibit immunogenic properties
XX
PS   Claim 3; Figure 2; 100pp; English.
XX
CC   The isolation and purification of the high molecular weight protein
CC   enables the identification of the major protective epitopes of the
CC   protein by conventional epitope mapping.  These epitopes can then be
CC   synthesised using standard techniques and incorporated into fully
CC   synthetic or recombinant vaccines.
XX
SQ   Sequence   1536 AA;


alignment_scores:
           Quality:  272.50              Length:   1182
             Ratio:  0.452                Gaps:     60
 Percent Similarity:  51.015   Percent Identity: 20.897

alignment_block:
 US-09-303-518D-649 x AAR41723   ..

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         |||:::||||||:::|||                              :::::
     349 GlyGluThrTyrLeuGly.........................GlyAs 356

     177 AAATAAAGGCAAGTTTGCAGTCGGGGCGAAAGATATTGAGGTTTACAACA 226
         :::::::|||:::          |||   :::   |||::::::   :::|
     356 pGluArgGlyGlu.........GlyLysAsnGlyIleGlnLeuAlaLysL 370

     227 AAAAAGGGGAGTTGGTCGGCAAATCAATGACAAAAGCCCCGATGATTGAT 276
         ||                        |||:::   |||:::      |||:::
     370 ys..................ThrSerLeuGluLysGlySerThrIleAsn 380

     277 TTTTCTGTGGTGTCGCGTAACGGCGTGGCGGCATTGGTGGGCGATCAATA 326
            |||      ::::::::::|||   |||   :::   ||||||
     381 ValSerGlyLysGluLysGlyGlyArgAlaIleValTrpGlyAspIleAl 397

     327 TATTGTG..............................AGCGTGGCACATA 346
          ::::::                            ::::::|||   :
     397 aLeuIleAspGlyAsnIleAsnAlaGlnGlySerGlyAspIleAlaLysT 414

     347 ACGGCGGC..................................... 354
         ::|||||
     414 hrGlyGlyPheValGluThrSerGlyHisAspLeuPheIleLysAspAsn 430

     355 ...............................TATAACAACGTTGATTT 371
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                                                  :::::::||||||:::::
431 AlaIleValAspAlaLysGluTrpLeuLeuAspPheAspAsnValSerIl 447

372 TGGTGCGGAA......GGAAGAAATCCCGATCAACATCGTTTTACTTAT. 414
    ::::||||||      ||||||:::      ::::::         |||
447 eAsnAlaGluThrAlaGlyArgSerAsnThrSerGluAspAspGluTyrT 464

415 ....................AAAATTGTGAAACGGAATAATTATAAAGCA 444
                        :::      ||||||||||:::   |||:::
464 hrGlySerGlyAsnSerAlaSerThrProLysArgAsnLysGluLysThr 480

445 GGGACTAAAGGCCATCCTTATGGCGGCGATTATCATATGCCGCGTTTGCA 494
       |||              :::   :::|||:::       :::   :
481 .ThrLeuThrAsnThrThrLeuGluSerIleLeuLysLysGlyThrPheV 497

495 TAAATTTGTCACAGATGCAGAACCTGTTGAAATGACCAGTTATATGGATG 544
    ::|||::::::      |||:::                  |||::::::
497 alAsnIleThrAlaAsnGlnArg.................IleTyrVal 507

545 GGCGGAAATATATCGATCAAAATAATTACCCTGACCGTGTTCGTATTGGG 594
    :::::::::|||:::::::::      :::||||||::::::      ||
508 AsnSerSerIleAsnLeuSerAsnGlySerLeuThrLeuTrpSerGluGl 524

595 GCAGGCAGGC..........................AATATTGGCGATC 617
    |:::::::|||                        :::   ||||||
524 yArgSerGlyGlyGlyValGluIleAsnAsnAspIleThrThrGlyAspA 541

618 TGATGAAGATGAGCCCAATAACC.................GCGAAAGTT 649
       :::   :::   :::|||                   :::   |||
541 spThrArgGlyAlaAsnLeuThrIleTyrSerGlyGlyTrpValAspVal 557

650 CATATCATATTGCAAGTGCGTATTCTTGGCTCGTTGGTGGCAATACCTTT 699
    |||      :::::::::         |||:::::  :::   |||
558 HisLysAsnIleSerLeuGlyAlaGlnGlyAsnIle..AsnIleThrAla 573

700 GCACAAAAT..............GGATCA..............GGTGG 719
       |||:::              ||||||               |||
574 LysGlnAspIleAlaPheGluLysGlySerAsnGlnValIleThrGlyGl 590

720 TGGCACAGTCAACTTAGGTAGTGAAAAAATTAAACATAGCCCATATGGTT 769
     ||||||::::::   |||:::::|||                ||||
590 nGlyThrIleThrSerGlyAsnGlnLys.................GlyP 601

770 TTTTACCAACAGGAGGCTCATTTGGCGACAGTGGCTCACCAATGTTTATC 819
    ||      ::::::   |||:::::   :::|||||||   :::   :::
601 heArgPheAsnAsnValSerLeuAsnGlyThrGlySerGlyLeuGlnPhe 617

820 TATGATGCCCAAAAGCAAAAGTGGTTAATTAATGGGGTATTGCAAACGGG 869
              :::   :::|||:::   |||::::::   ::::::
618 ThrThrLysArgThrAsnLysTyrAlaIleThrAsnLysPheGluGlyTh 634

870 CAACCCCTATATAGGAAAAAGCAAT...GGCTTCCAGCTGGTTCGTAAAG 916
                  ||||||   |||   ::::::   |||   :::::::
634 rLeuAsnIleSerGlyLysValAsnIleSerMetValLeuProLysAsnG 651

917 ATTGGTTCTATGATGAAATCTTTGCTGGAGATACCCAT......TCAGTA 960
    ::      ||||||:::   |||   |||   |||:::         :::
651 luSerGlyTyrAspLys...PheLysGlyArgThrTyrTrpAsnLeuThr 666

961 TTCTACGAACCACGTCAAAATGGGAAATACTCTTTTAACGACGATAATAA 1010
       :::      ::::::|||:::::::::::::::   |||:::::
667 SerLeuAsnValSerGluSerGlyGluPheAsnLeuThrIleAspSerAr 683

1011 TGGCACA.........GGAAAAATCAATGCCAAACATGAACACAATTCTC 1051
     :|||:::         |||   ::::::      :::::::   ||||:::
683 gGlySerAspSerAlaGlyThrLeuThrGlnProTyrAsnLeuAsnGlyI 700

1052 TGCCT...AATAGATTAAAAACACGAACCGTTCAATTGTTTAATGTTTCT 1098
     ::      |||:::      |||   :::|||:::      |||:::
700 leSerPheAsnLysAspThrThrPheAsnValGluArg...AsnAlaArg 715

1099 TTATCCGAGACAGCAAGAGAACCTGTTTATCATGCTGCAGGTGGTGTCAA 1148
     ::::::         :::   |||:::               |||:::||
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716 ValAsnPheAspIleLysAlaProIle.............GlyIleAs 727

1149 CAGTTATCGACCCAGACTGAATAATGGAGAAAATATTTCCTTTATTGACG 1198
     |:::|||                 ::::::::::::::   :::
727 nLysTyr.....................SerSerLeuAsnTyrAlaSer. 736

1199 AAGGAAAAGGCGAATTGATACTTACCAGCAACATCAATCAAGGTGCTGGA 1248
                          :::::::::||||||:::   ::::::|||
737 ...................PheAsnGlyAsnIleSerValSerGlyGly 746

1249 GGATTATATTTCCAAGGAGATTTTACGGTCTCGCCTGAAAATAACGAAAC 1298
     |||          :::   ||||||||||:::      ::::::::::::::
747 Gly.........SerValAspPheThrLeuLeuAlaSerSerSerAsnVa 760

1299 TTGGCAAGGCGCGGGCGTT.....................CATATCAGTG 1327
     :   |||      ||||||                      ::::::|||
760 l...GlnThrProGlyValValIleAsnSerLysTyrPheAsnValSerT 776

1328 AAGACAGTACCGTTACTTGGAAAGTAAACGGC..................... 1359
          |||::::::   :::|||::::::|||
776 hrGlySerSerLeuArgPheLysThrSerGlySerThrLysThrGlyPhe 792

1360 ...GTGGCAAACGAC...CGCCTGTCCAAAATCGGCAAAGGCACGCTGCA 1403
        :::   :::|||      |||:::      |||   :::
793 SerIleGluLysAspLeuThrLeuAsnAlaThrGlyGlyAsnIleThrLe 809

1404 CGTTCAAGCCAAAGGGGAAAAC..........................C 1426
      :::|||::::::|||   :::                          :
809 uLeuGlnValGluGlyThrAspGlyMetIleGlyLysGlyIleValAlaL 826

1427 AAGGCTCGATCAGCGTGGGCGACGGTACAGTCATTTTGGATCAGCAGGCA 1476
     ::   :::|||:::          |||::::::   :::
826 ysLysAsnIleThrPheGluGlyGlyAsnIleThrPhe............ 838

1477 GACGATAAAGGCAAAAAACAAGCCTTTAGTGAAATCGGCTTGGTCAGCGG 1526
               |||::::::::::|||   :::||||||          :::||
839 .........GlySerArgLysAlaValThrGluIle.........GluGl 849

1527 CAGGGGTACGGTGCAACTGAATGCCGATAATCAGTTCAACCCCGACAAAC 1576
     |:::   |||::::::   ||||||:::
849 yAsnValThrIleAsnAsnAsnAlaAsn..................... 858

1577 TCTATTTCGGCTTTCGCGGCGGACGTTTGGATTTAAACGGGCATTCGCTT 1626
                                  :::   |||   |||   ::::::
859 ........................ValThrLeuIleGlySerAspPhe 866

1627 TCGTTCCACCGTATTCAAAATACCGATGAAGGGGCGATGATTGTCAACCA 1676
     :::   |||:::         |||   :::      :::|||:::|||
867 AspAsnHisGlnLysProLeuThrIleLeuLysLysAspValIleIleAsnSe 883

1677 CAATCAA......GACAAAGAATCCACCGTTACCATTACAGGCAATAAAG 1720
      ::::::               :::   |||:::|||:::|||||||
883 rGlyAsnLeuThrAlaGlyGlyAsnIleValAsnIleAlaGlyAsnLeuT 900

1721 ATATTGCTACAACCGGCAAT.....................................  1740
       :::   :::::::::|||
900 hrValGluSerAsnAlaAsnPheLysAlaIleThrAsnPheThrPheAsn 916

1741 ..............AACAACAGCTTGGATAGCAAAAAAGAAATTGCCTA 1775
                    :::|||:::   :::|||:::   :::||||||
917 ValGlyGlyLeuPheAspAsnLysGlyAsnSerAsnIleSerIleAlaLy 933

1776 CAACGGT...TGGTTTGGCGAGAAAGATACGACCAAAACGAACGGGCGGC 1822
      :::|||      |||   :::   |||:::::|||          :::|
933 sGlyGlyAlaArgPheLysAspIleAspAsnSerLys.........AsnL 947

1823 TCAACCTTGTTTACCAGCCCGCCGCAGAAGACCGCACCCTGCTGCTTTCC 1872
     ||::::::::::   :::   ::::::      ||||||::::::   :::
947 euSerIleThrThrAsnSerSerSerThrTyrArgThrIleIleSerGly 963

1873 GGCGGAACAAATTTAAACGGCAACATCACGCAAACAAACGGCAAACTGTT 1922
     :::   ||||||   ||||||::::::::::   ||||||
964 AsnIleThrAsnLysAsnGlyAspLeuAsnIleThrAsn............ 976
```

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1923 TTTCAGCGGCAGACCAACACCGCACGCCTACAATCATTTAAACGACCATT 1972
977 ....GluGlySerAspThrGlu.....MetGlnIleGlyGlyAspV 989

1973 GGTCGCAAAAAGAGGGCATTCCTCGCGGGGAAATCGTGTGGGACAACGAC 2022
989 alSerGlnLysGlu.....GlyAsnLeuThrIleSerSerAsp 1001

2023 TGGATCAACCGCACATTTAAAGCGGAAAACTTCCAAATTAAAGGCGGACA 2072
1002 LysIleAsnIleThr.....LysGlnIleThrIleLysAlaGly.. 1014

2073 GGCGGTGGTTTCCCGCAATGTTGCCAAAGTGAAAGGCGATTGGCATTTGA 2122
1015 .....ValAspGlyGluAsnSerAspSerAspAlaT 1025

2123 GCAATCACGCCCAAGCAGTTTTTGGTGTCGCACCGCATCAAAGCCACACA 2172
1025 hrAsnAsnAlaAsnLeu.....Thr 1031

2173 ATCTGTACACGTTCGGACTGGACGGGTCTGACAAATTGTGTCGAAAAAAC 2222
1032 IleLysThrLys.....GluLeuLy 1038

2223 CATTACCGACGATAAAGTGATTGCTTCATTGACTAAGACCGACATCAGCG 2272
1038 sLeuThrGlnAspLeuAsnIleSerGlyPheAsnLysAlaGluIleThrA 1055

2273 GCAATGTCGATCTTGCCGATCACGCTCATTTAAATCTCACAGGGCTTGCC 2322
1055 laLys...AspGlySerAsp.....Leu 1061

2323 ACACTCAACGGCAATCTTAGTGCAAATGGCGATACACGTTATACAGTCAG 2372
1062 ThrIleGlyAsnThrAsnSerAlaAspGlyThrAsnAlaLysLysValTh 1078

2373 CCACAACGCCACCCAAAACGGCAACCTTAGCCTCGTGGGCAATGCCCAAG 2422
1078 rPheAsnGlnValLysAspSerLysIleSerAlaAspGly..... 1091

2423 CAACATTTAATCAAGCCACATTAAACGGCAACACATCGGCTTCGGGCAAT 2472
1092 .....HisLysValThrLeuHisSerLysValGluThrSerGlySer 1105

2473 GCTTCATTTAATCTAAGCGACCACGCCGTACAAAACGGCAGTCTGACGCT 2522
1106 AsnAsn...AsnThrGluAspSerSerAspAsnAsnAlaGlyLeuThrIl 1121

2523 TTCCGGCAACGCTAAGGCAAACGTAAGCCATTCCGCACTCAACGGTAATG 2572
1121 e.....AspAlaLys...AsnValThr.....ValAsnAsnAsnI 1132

2573 TCTCCCTAGCCGATAAGGCAGTATTCCATTTTGAAAGCAGCCGCTTTACC 2622
1132 leThr...SerHisLysAlaVal.....SerIleSerAlaThrSer 1144

2623 GGACAAATCAGCGGCGGCAAGGATACGGCATTACACTTAAAA.....GA 2666
1145 GlyGluIleThrThrLysThrGlyThrThrIleAsnAlaThrThrGlyAs 1161

2667 CAGCGAATGGACGCTGCCGTCAGGCACGGAATTAGGCAATTTAAACCTTG 2716
1161 nValGluIleThrAlaGlnThrGlySerIleLeuGlyGlyIleGluSerS 1178

2717 ACAACGCCACCATTACACTCAATTCCGCCTATCGCCACGATGCGGCAGGG 2766
1178 erSerGlySerValThrLeuThrAlaThrGluGlyAlaLeuAlaValSer 1194

2767 GCGCAAACCGGCAGTGCGACAGATGCGCCGCGCCGCCGTTCGCGCCGTTC 2816
1195 AsnIleSerGlyAsnThrValThrValThrAlaAsnSerGlyAlaLeuTh 1211

2817 GCGCCGTTCCCTATTATCCGTTACACCGCCAACTTCGGTAGAATCCCGTT 2866
1211 rThrLeuAlaGlySerThrIleLysGlyThrGluSerValThrThrSerS 1228

2867 TCAACACGCTGACGGTAAACGGCAAATTGAACGGTCAGGGAACA..... 2910
1228 erGlnSerGlyAspIleGlyGlyThrIleSerGly...GlyThrValGlu 1243

2911 TTCCGCTTTATGTCGGAACTCTTCGGCTACCGCAGCGACAAATTGAAGCT 2960
1244 ValLysAlaThrGluSerLeuThrThrGlnSerAsnSerLysIleLys.. 1259

2961 GGCGGAAAGTTCCGAAGGCACTTACACCTTGGCGGTC..... 2997
1260 .AlaThrThrGlyGluAlaAsnValThrSerAlaThrGlyThrIleGlyG 1276

2998 .....AACAATACCGGCAACGAACCTGCAAGCCTCGAACAATTG 3036
1276 lyThrIleSerGlyAsnThrValAsnValThrAlaAsnAlaGlyAspLeu 1292

3037 ACGGTA.....GTGGAAGGAAAAGACAACAA 3062
1293 ThrValGlyAsnGlyAlaGluIleAsnAlaThrGluGlyAlaAlaThrLe 1309

3063 ACCGCTGTCCGAAAACCTTAATTTCACCCTGCAAAACGAACACGTCGATG 3112
1309 uThrThrSerSerGlyLysLeuThrThrGluAlaSerSerHisIleThrS 1326

3113 CCGGCGCGTGGCGTTACCAACTCATCCGCAAAGACGGCGAGTTCCGCCTG 3162
1326 er.AlaLysGlyGlnValAsnLeuSerAlaGlnAspGlySerValAlaGl 1342

3163 CATAATCCGGTCAAAGAACAAGAGCTTTCCGACAAACTCGGCAAGGCAGA 3212
1342 ySerIleAsnAlaAlaAsnValThrLeuAsnThrThrGlyThrLeuThrT 1359

3213 AGCCAAAAAACAGGCGGAAAAAGACAACGCGCAAAGCCTTG 3253
1359 hrValLysGlySerAsnIleAsnAlaThrSerGlyThrLeu 1372
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seq_documentation_block:
ID   AAW30293 standard; Protein; 1536 AA.
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AC   AAW30293;
XX
DT   14-APR-1998  (first entry)
XX
DE   Non-typeable Haemophilus high mol.wt. surface protein HMW1.
XX
KW   Non-typeable Haemophilus; high molecular weight surface protein;
KW   HMW1; hmw1A gene; immunogen; vaccine; otitis media.
XX
OS   Haemophilus influenzae strain 12.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 4
FT                   /note= "encoded by CTA"
FT   Misc-difference 98
FT                   /note= "encoded by GAT"
FT   Misc-difference 363
FT                   /note= "encoded by AAG"
XX
PN   WO9736914-A1.
XX
PD   09-OCT-1997.
XX
PF   01-APR-1997;   97WO-US04707.
XX
PR   01-APR-1996;   96US-0617697.
XX
PA   (BARE/) BARENKAMP S J.
```

XX
PI Barenkamp SJ;
XX
DR WPI; 1997-503038/46.
DR N-PSDB; AAT90994 and AAT90996.
XX
PT High molecular weight proteins of non-typeable Haemophilus
PT influenzae - useful for vaccine production
XX
PS Claim 7; Page 66-70; 183pp; English.
XX
CC This protein comprises the high molecular weight surface protein
CC HMW1 (125 kDa) of non-typeable Haemophilus influenzae strain 12 that
CC has the immunological ability to protect against disease caused by a
CC non-typeable Haemophilus strain and is characterised by at least
CC one surface-exposed B-cell epitope that is recognised by monoclonal
CC antibody AD6. The HMW1 amino acid sequence was deduced from the
CC hmw1 gene sequence (see AAT90994 and AAT90996). The expressed protein
CC is truncated, starting at residue 442 of the full-length gene
CC product. HMW2 (see AAW30294), HMW3 (see AAW30291) and HMW4 (see
CC AAW30292) have also been identified. A conjugate comprising HMW1
CC linked to an antigen, hapten or polysaccharide, and a synthetic
CC peptide of 6-150 amino acids corresponding to at least protective
CC epitope of HMW1 are also claimed. HMW proteins, conjugates and
CC peptides can be used in vaccines, as immunogens for preparation of
CC antibodies and as antigens for detection of these antibodies.
XX
SQ Sequence 1536 AA;

alignment_scores:
Quality: 269.50 Length: 1190
Ratio: 0.452 Gaps: 60
Percent Similarity: 50.084 Percent Identity: 20.840

alignment_block:
US-09-303-518D-649 x AAW30293 ..

Align seg 1/1 to: AAW30293 from: 1 to: 1536

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127 GGACACACTTATTTCGGCATCAACTACCAATACTATCGCGACTTTGCCGA 176
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349 GlyGluThrTyrLeuGly.........................GlyAs 356

177 AAATAAAGGCAAGTTTGCAGTCGGGGCGAAAGATATTGAGGTTTACAACA 226
    :::::::|||:::          |||   :::   |||::::::   :::|
356 pGluArgGlyGlu.........GlyLysAsnGlyIleGlnLeuAlaLysL 370

227 AAAAAGGGGAGTTGGTCGGCAAATCAATGACAAAAGCCCCGATGATTGAT 276
    ||                        |||:::   |||:::      |||:::
370 ys..................ThrSerLeuGluLysGlySerThrIleAsn 380

277 TTTTCTGTGGTGTCGCGTAACGGCGTGGCGGCATTGGTGGGCGATCAATA 326
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381 ValSerGlyLysGluLysGlyGlyArgAlaIleValTrpGlyAspIleAl 397

327 TATTGTG............................AGCGTGGCACATA 346
     ::::::                          ::::::|||   :
397 aLeuIleAspGlyAsnIleAsnAlaGlnGlySerGlyAspIleAlaLysT 414

347 ACGGCGGCTAT..................................... 357
    ::||||||:::
414 hrGlyGlyPheValGluThrSerGlyHisAspLeuPheIleLysAspAsn 430

358 ..................................AACAACGTTGATTT 371
                                      :::|||||||:::::
431 AlaIleValAspAlaLysGluTrpLeuLeuAspProAspAsnValSerIl 447

372 TGGTGCGGAA......GGAAGAAATCCCGATCAACATCGTTTTACTTAT. 414
    ::::||||||     ||||||:::     ::::::         |||
447 eAsnAlaGluThrAlaGlyArgSerAsnThrSerGluAspAspGluTyrT 464

415 ..................AAAATTGTGAAACGGAATAATTATAAAGCA 444

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464 hrGlySerGlyAsnSerAlaSerThrProLysArgAsnLysGluLysThr 480

445 GGGACTAAAGGCCATCCTTATGGCGGCGATTATCATATGCCGCGTTTGCA 494
       |||            :::   :::|||:::        :::   :
481 .ThrLeuThrAsnThrThrLeuGluSerIleLeuLysLysGlyThrPheV 497

495 TAAATTTGTCACAGATGCAGAACCTGTTGAAATGACCAGTTATATGGATG 544
    ::|||::::::     |||:::                  |||::::::
497 alAsnIleThrAlaAsnGlnArg.................IleTyrVal 507

545 GGCGGAAATATATCGATCAAAATAATTACCCTGACCGTGTTCGTATTGGG 594
    :::::::::|||:::::::::     :::|||||:::::      ||
508 AsnSerSerIleAsnLeuSerAsnGlySerLeuThrLeuTrpSerGluGl 524

595 GCAGGCAGGC.........................AATATTGGCGATC 617
    |:::::::|||                       :::   ||||||
524 yArgSerGlyGlyGlyValGluIleAsnAsnAspIleThrThrGlyAspA 541

618 TGATGAAGATGAGCCCAATAACC.................GCGAAAGTT 649
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541 spThrArgGlyAlaAsnLeuThrIleTyrSerGlyGlyTrpValAspVal 557

650 CATATCATATTGCAAGTGCGTATTCTTGGCTCGTTGGTGGCAATACCTTT 699
    |||      :::::::::         |||::::::  :::   |||
558 HisLysAsnIleSerLeuGlyAlaGlnGlyAsnIle..AsnIleThrAla 573

700 GCACAAAAT..............GGATCA..............GGTGG 719
       |||:::              ||||||               |||
574 LysGlnAspIleAlaPheGluLysGlySerAsnGlnValIleThrGlyGl 590

720 TGGCACAGTCAACTTAGGTAGTGAAAAAATTAAACATAGCCCATATGGTT 769
     ||||||::::::   |||:::::::|||                ||||
590 nGlyThrIleThrSerGlyAsnGlnLys.................GlyP 601

770 TTTTACCAACAGGAGGCTCATTTGGCGACAGTGGCTCACCAATGTTTATC 819
    ||      ::::::   |||::::::   :::||||||   :::   :::
601 heArgPheAsnAsnValSerLeuAsnGlyThrGlySerGlyLeuGlnPhe 617

820 TATGATGCCCAAAAGCAAAAGTGGTTAATTAATGGGGTATTGCAAACGGG 869
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618 ThrThrLysArgThrAsnLysTyrAlaIleThrAsnLysPheGluGlyTh 634

870 CAACCCCTATATAGGAAAAAGCAAT...GGCTTCCAGCTGGTTCGTAAAG 916
                  ||||||   |||   ::::::   |||   :::::::
634 rLeuAsnIleSerGlyLysValAsnIleSerMetValLeuProLysAsnG 651

917 ATTGGTTCTATGATGAAATCTTTGCTGGAGATACCCAT......TCAGTA 960
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651 luSerGlyTyrAspLys...PheLysGlyArgThrTyrTrpAsnLeuThr 666

961 TTCTACGAACCACGTCAAAATGGGAAATACTCTTTTAACGACGATAATAA 1010
          :::      :::::::|||:::::::::::::::   |||:::::
667 SerLeuAsnValSerGluSerGlyGluPheAsnLeuThrIleAspSerAr 683

1011 TGGCACA.........GGAAAAATCAATGCCAAACATGAACACAATTCTC 1051
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683 gGlySerAspSerAlaGlyThrLeuThrGlnProTyrAsnLeuAsnGlyI 700

1052 TGCCT...AATAGATTAAAAACACGAACCGTTCAATTGTTTAATGTTTCT 1098
     ::      |||:::      |||   :::|||:::      |||:::
700 leSerPheAsnLysAspThrThrPheAsnValGluArg...AsnAlaArg 715

1099 TTATCCGAGACAGCAAGAGAACCTGTTTATCATGCTGCAGGTGGTGTCAA 1148
     ::::::         :::   |||:::               |||:::||
716 ValAsnPheAspIleLysAlaProIle.............GlyIleAs 727

1149 CAGTTATCGACCCAGACTGAATAATGGAGAAAATATTTCCTTTATTGACG 1198
     |:::|||                        :::::::::::::::   :::
727 nLysTyr...................SerSerLeuAsnTyrAlaSer. 736

1199 AAGGAAAAGGCGAATTGATACTTACCAGCAACATCAATCAAGGTGCTGGA 1248
                          :::::::::|||||||:::   ::::::|||
```

```
 737 ...................PheAsnGlyAsnIleSerValSerGlyGly 746

1249 GGATTATATTTCCAAGGAGATTTTACGGTCTCGCCTGAAAATAACGAAAC 1298
     |||          :::   |||||||||:::      :::::::::::::
 747 Gly.........SerValAspPheThrLeuLeuAlaSerSerSerAsnVa 760

1299 TTGGCAAGGCGCGGGCGTT.....................CATATCAGTG 1327
     :   |||      ||||||                      :::::::|||
 760 l...GlnThrProGlyValValIleAsnSerLysTyrPheAsnValSerT 776

1328 AAGACAGTACCGTTACTTGGAAAGTAAACGGC..................... 1359
          |||::::::   :::|||::::::|||
 776 hrGlySerSerLeuArgPheLysThrSerGlySerThrLysThrGlyPhe 792

1360 ...GTGGCAAACGAC...CGCCTGTCCAAAATCGGCAAAGGCACGCTGCA 1403
        :::   :::|||      |||:::      |||   :::
 793 SerIleGluLysAspLeuThrLeuAsnAlaThrGlyGlyAsnIleThrLe 809

1404 CGTTCAAGCCAAAGGGGAAAAC.........................C 1426
      :::|||:::::::|||   :::                       :
 809 uLeuGlnValGluGlyThrAspGlyMetIleGlyLysGlyIleValAlaL 826

1427 AAGGCTCGATCAGCGTGGGCGACGGTACAGTCATTTTGGATCAGCAGGCA 1476
     ::   :::|||:::         |||::::::   :::
 826 ysLysAsnIleThrPheGluGlyGlyAsnIleThrPhe............ 838

1477 GACGATAAAGGCAAAAAACAAGCCTTTAGTGAAATCGGCTTGGTCAGCGG 1526
           |||::::::::::|||   :::||||||         :::||
 839 .........GlySerArgLysAlaValThrGluIle.........GluGl 849

1527 CAGGGGTACGGTGCAACTGAATGCCGATAATCAGTTCAACCCCGACAAAC 1576
     |:::   |||::::::   ||||||:::
 849 yAsnValThrIleAsnAsnAsnAlaAsn..................... 858

1577 TCTATTTCGGCTTTCGCGGCGGACGTTTGGATTTAAACGGGCATTCGCTT 1626
                           :::   |||   |||   ::::::
 859 ........................ValThrLeuIleGlySerAspPhe 866

1627 TCGTTCCACCGTATTCAAAATACCGATGAAGGGGCGATGATTGTCAACCA 1676
     :::   |||:::      |||   :::     :::|||:::|||
 867 AspAsnHisGlnLysProLeuThrIleLysLysAspValIleIleAsnSe 883

1677 CAATCAA......GACAAAGAATCCACCGTTACCATTACAGGCAATAAAG 1720
      ::::::                :::   |||:::|||:::||||||
 883 rGlyAsnLeuThrAlaGlyGlyAsnIleValAsnIleAlaGlyAsnLeuT 900

1721 ATATTGCTACAACCGGCAAT.............................. 1740
       :::   :::::::::|||
 900 hrValGluSerAsnAlaAsnPheLysAlaIleThrAsnPheThrPheAsn 916

1741 ..............AACAACAGCTTGGATAGCAAAAAAGAAATTGCCTA 1775
                    :::|||:::   :::|||:::   :::||||||
 917 ValGlyGlyLeuPheAspAsnLysGlyAsnSerAsnIleSerIleAlaLy 933

1776 CAACGGT...TGGTTTGGCGAGAAAGATACGACCAAAACGAACGGGCGGC 1822
      :::|||      |||   :::   |||:::::::|||         :::|
 933 sGlyGlyAlaArgPheLysAspIleAspAsnSerLys.........AsnL 947

1823 TCAACCTTGTTTACCAGCCCGCCGCAGAAGACCGCACCCTGCTGCTTTCC 1872
     ||:::::::::   :::   ::::::      ||||||::::::   :::
 947 euSerIleThrThrAsnSerSerSerThrTyrArgThrIleIleSerGly 963

1873 GGCGGAACAAATTTAAACGGCAACATCACGCAAACAAACGGCAAACTGTT 1922
     :::   ||||||   ||||||:::::::::   ||||||
 964 AsnIleThrAsnLysAsnGlyAspLeuAsnIleThrAsn........... 976

1923 TTTCAGCGGCAGACCAACACCGCACGCCTACAATCATTTAAACGACCATT 1972
        :::|||      |||                 :::::::::
 977 ....GluGlySerAspThrGlu.........MetGlnIleGlyGlyAspV 989

1973 GGTCGCAAAAAGAGGGCATTCCTCGCGGGGAAATCGTGTGGGACAACGAC 2022
       ||||||||||||           |||::::::::   ::::::|||
 989 alSerGlnLysGlu............GlyAsnLeuThrIleSerSerAsp 1001

2023 TGGATCAACCGCACATTTAAAGCGGAAAACTTCCAAATTAAAGGCGGACA 2072
        ||||||   |||         :::::::::   ||||||:::|||
1002 LysIleAsnIleThr.........LysGlnIleThrIleLysAlaGly.. 1014

2073 GGCGGTGGTTTCCCGCAATGTTGCCAAAGTGAAAGGCGATTGGCATTTGA 2122
                        |||         :::::::|||         :
1015 ...................ValAspGlyGluAsnSerAspSerAspAlaT 1025

2123 GCAATCACGCCCAAGCAGTTTTTGGTGTCGCACCGCATCAAAGCCACACA 2172
     ::|||:::|||:::                                  |||
1025 hrAsnAsnAlaAsnLeu.............................Thr 1031

2173 ATCTGTACACGTTCGGACTGGACGGGTCTGACAAATTGTGTCGAAAAAAC 2222
     |||   |||:::                                  |||
1032 IleLysThrLys.............................GluLeuLy 1038

2223 CATTACCGACGATAAAGTGATTGCTTCATTGACTAAGACCGACATCAGCG 2272
      :::|||:::|||      |||:::::::::::::|||::::::|||::::
1038 sLeuThrGlnAspLeuAsnIleSerGlyPheAsnLysAlaGluIleThrA 1055

2273 GCAATGTCGATCTTGCCGATCACGCTCATTTAAATCTCACAGGGCTTGCC 2322
     :::::   |||   :::|||
1055 laLys...AspGlySerAsp.........................Leu 1061

2323 ACACTCAACGGCAATCTTAGTGCAAATGGCGATACACGTTATACAGTCAG 2372
     |||::::::::::::   ||||||:::|||   :::         |||::
1062 ThrIleGlyAsnThrAsnSerAlaAspGlyThrAsnAlaLysLysValTh 1078

2373 CCACAACGCCACCCAAAACGGCAACCTTAGCCTCGTGGGCAATGCCCAAG 2422
     :   |||   :::::::::::::::::::|||      |||:::      :
1078 rPheAsnGlnValLysAspSerLysIleSerAlaAspGlyHisLysValT 1095

2423 CAACATTTAATCAAGCCACATTAAACGGCAACACATCGGCTTCGGGCAAT 2472
     ::      :::::::::      :::|||:::::::::   :::   :::
1095 hrLeuHisSerLysValGluThrSerGlySerAsnAsnAsnThrGluHis 1111

2473 GCTTCATTTAATCTAAGCGACCACGCCGTACAAAACGGCAGTCTGACGCT 2522
     :::|||   |||   :::      :::::::::      ::::::|||::
1112 SerSerAspAsnAsnAlaGlyLeuThrIleAspAlaLysAsnValThrVa 1128

2523 TTCCGGCAACGCTAAGGCAAAC......GTAAGCCATTCCGCACTCAACG 2566
     ::::::::|||      ::::::      ||||||   ||||||   :::|
1128 lAsnAsnAsnIleThrSerHisLysAlaValSerIleSerAlaThrSerG 1145

2567 GTAATGTC..............TCCCTAGCCGATAAGGCAGTATTCCAT 2601
     ||::::::                :::      :::   ::::::   :::
1145 lyGluIleThrThrLysThrGlyThrThrIleAsnAlaThrThrGlyAsn 1161

2602 TTTGAAAGCAGCCGCTTTACCGGACAAATCAGCGGCGGCAAGGATACG.. 2649
        |||   :::      ||||||:::|||   ||||||   ::::::
1162 ValGluIleThrAlaGlnThrGlySerIleLeuGlyGlyIleGluSerSe 1178

2650 .......GCATTACACTTAAAAGACAGCGAATGGACGCTGCCGTCAGGCA 2692
             ::::::   |||       :::|||   :::|||
1178 rSerGlySerValThrLeuThrAlaThrGluGlyAlaLeu......... 1191

2693 CGGAATTAGGCAATTTAAACCTTGACAACGCCACCATTACACTCAATTCC 2742
          ::::::|||::::::   :::::::::|||:::|||   ||||||
1192 ..AlaValSerAsnIleSerGlyAsnThrValThrValThrAlaAsnSer 1207

2743 GCCTATCGCCACGATGCGGCAGGGGCGCAAACCGGCAGTGCGACAGATGC 2792
     :::                 ||||||:::   |||   ::::::|||:::
1208 GlyAlaLeuThrThrLeuAlaGlySer...ThrIleLysGlyThrGlu.. 1222

2793 GCCGCGCCGCCGTTCGCGCCGTTCGCGCCGTTCCCTATTATCCGTTACAC 2842
                                             |||||||||
1223 .....................................SerValThr. 1225

2843 CGCCAACTTCGGTAGAATCCCGTTTCAACACGCTGACGGTAAACGGCAAA 2892
          ||||||   :::|||                 :::::|||
1226 .....ThrSerSerGlnSerGly............AspIleGlyGlyThr 1236
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    2893 TTGAACGGTCAGGGAACA......TTCCGCTTTATGTCGGAACTCTTCGG 2936
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    1237 IleSerGly...GlyThrValGluValLysAlaThrGluSerLeuThrTh 1252

    2937 CTACCGCAGCGACAAATTGAAGCTGGCGGAAAGTTCCGAAGGCACTTACA 2986
                :::::|||:::|||   |||   ::::::|||:::::   |
    1252 rGlnSerAsnSerLysIleLys...AlaThrThrGlyGluAlaAsnValT 1268

    2987 CCTTGGCGGTC.......................AACAATACCGGCAAC 3012
         ||   |||:::                      :::|||||| ' |||
    1268 hrSerAlaThrGlyThrIleGlyGlyThrIleSerGlyAsnThrValAsn 1284

    3013 GAACCTGCAAGCCTCGAACAATTGACGGTA..................... 3042
              |||:::      :::|||||||||
    1285 ValThrAlaAsnAlaGlyAspLeuThrValGlyAsnGlyAlaGluIleAs 1301

    3043 ....GTGGAAGGAAAAGACAACAAACCGCTGTCCGAAAACCTTAATTTCA 3088
             :::|||||      :::         |||::::::         |
    1301 nAlaThrGluGlyAlaAlaThrLeuThrThrSerSerGlyLysLeuThrT 1318

    3089 CCCTGCAAAACGAACACGTCGATGCCGGCGCGTGGCGTTACCAACTCATC 3138
         ||      :::::|||:::   ::: |||:::|||   :::|||   ||
    1318 hrGluAlaSerSerHisIleThrSer.AlaLysGlyGlnValAsnLeuSe 1334

    3139 CGCAAAGACGGCGAGTTCCGCCTGCATAATCCGGTCAAAGAACAAGAGCT 3188
         ||||:::   :::|||   |||      |||::::::   |||   ::::
    1334 rAlaGlnAspGlySerValAlaGlySerIleAsnAlaAlaAsnValThrL 1351

    3189 TTCCGACAAACTCGGCAAGGCAGAAGCCAAAAAACAGGCGGAAAAAGACA 3238
         ::   |||::::::::::           |||:::   :::   ::::::
    1351 euAsnThrThrGlyThrLeuThrThrValLysGlySerAsnIleAsnAla 1367

    3239 ACGCGCAAAGCCTTG 3253
         |||      :::|||
    1368 ThrSerGlyThrLeu 1372
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seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2000.DAT:AAB01837

seq_documentation_block:

```
ID   AAB01837 standard; Protein; 1073 AA.
XX
AC   AAB01837;
XX
DT   11-SEP-2000  (first entry)
XX
DE   Haemophilus influenzae strain LCDC2 mature HMW2A protein, SEQ ID NO:49.
XX
KW   Mature HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW   non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW   recombinant production; Escherichia coli; antibacterial; vaccine;
KW   human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW   detection; diagnosis.
XX
OS   Haemophilus influenzae strain LCDC2.
XX
PN   WO200020609-A2.
XX
PD   13-APR-2000.
XX
PF   07-OCT-1999;   99WO-CA00938.
XX
PR   07-OCT-1998;   98US-0167568.
PR   08-DEC-1998;   98US-0206942.
XX
PA   (CONN-) CONNAUGHT LAB LTD.
XX
PI   Loosmore SM,  Yang Y,  Klein MH;
XX
DR   WPI; 2000-303789/26.
DR   N-PSDB; AAA52186.
XX
PT   Nucleic acid molecule for producing recombinant high molecular weight
PT   proteins of Haemophilus which are used as a vaccine to provide
PT   protection against Haemophilus induced diseases in humans -
XX
PS   Claim 8; Fig 23A-P; 307pp; English.
XX
CC   The invention relates to the recombinant production of Haemophilus
CC   influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC   expression construct used to effect recombinant expression comprises a
CC   promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC   to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC   influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC   clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC   hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC   and the hmwB and hmwC genes encode accessory proteins which are
CC   responsible for post-translational processing and secretion of the HMWA
CC   proteins. The modified hmwABC operon used in the expression construct of
CC   the invention contains an A gene modified such that it encodes only the
CC   mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC   and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC   strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC   vectors are used for the production of recombinant H. influenzae HMW
CC   proteins which can be used as vaccines to mediate a humoral or
CC   cell-mediated immune response to provide protection against diseases in
CC   humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC   pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC   antigens in immunoassays for detecting antibodies against Haemophilus,
CC   HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC   HMW proteins can be used to isolate and clone hmw genes from other
CC   non-typeable strains of Haemophilus via hybridisation reactions. The
CC   present sequence represents a mature HMWA protein from a non-typeable
CC   strain of H. influenzae.
XX
SQ   Sequence   1073 AA;
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alignment_scores:

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            Quality:  268.00              Length:   1062
              Ratio:  0.485                 Gaps:     53
 Percent Similarity:  52.072   Percent Identity: 20.716
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alignment_block:

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 Align seg 1/1  to: AAB01837  from: 1  to: 1073

     787 TCATTTGGCGACAGTGGCTCACCAATGTTTATCTATGATGCCCAAAAGCA 836
         ::::::||||||||||||      :::   :::|||      :::|||::
      72 AsnIleGlyAspSerGlyHis...LeuThrLeuTyrLysLysArgLysAs 87

     837 AAAGTGGTTAATTAATGGGGTATTGCAAACGGGCAACCCCTATATAGGAA 886
         ::::         :::      :::|||   ::::::          :::
      87 nArg.........SerAspGlyIleGlnIleAsnLysAspIleThrSerT 101

     887 AAAGCAATGGCTTCCAGCTGGTTCGTAAAGATTGG......TTCTATGAT 930
           ::::::::::::   :::         ||||||      ::::::
     101 hrGlyGlySerLeuThrIleAsnSerAspAspTrpValAspIleHisGly 117

     931 GAAATCTTTGCTGGAGAT.....................ACCCATTCAGT 959
         :::|||      |||:::                     :::   |||||
     118 AsnIleThrLeuGlyGluGlyPheLeuAsnIleThrSerSerAspServa 134

     960 ATTCTACGAA..................................... 969
         |   :::|||
     134 lAlaPheGluGlyGlyAsnGlyAsnLysGlyArgSerSerAlaSerAlaG 151

     970 ............................CCACGTCAAAATGGGAAATAC 990
                                      :::|||      :::
     151 lnIleIleAlaGlnGlyThrIleThrLeuThrGlyGluAsnLysThrPhe 167

     991 TCTTTTAACGACGATAAT...AATGGCACAGGAAAA...ATCAATGCCAA 1034
           :::|||:::   :::   ||||||||||||:::   ::::::
     168 ArgLeuAsnAsnValSerLeuAsnGlyThrGlyAsnGlyLeuSerIleIl 184

    1035 ACATGAACACAATTCTCTGCCTAATAGATTAAAAACACGAACCGTTCAAT 1084
```

```
                :::::::|||   :::||||||      :::
 184 eSerThrAlaSerAsnLeuSerHisArgLeuAspGlyGluIleAsnValS 201

1085 TGTTTAATGTTTCTTTATCCGAGACAGCAAGAGAACCTGTT...TATCAT 1131
       ||||||:::::::::::::|||:::::::::   :::   |||
 201 erGlyAsnValThrIleAsnGlnThrThrGlnGlnAsnIleGluTyrTrp 217

1132 GCTGCAGGT..............GGTGTCAACAGTTATCGACCCAGA.. 1164
       |||:::                :::|||:::|||:::::   |||
 218 LysAlaSerSerAspSerTyrTrpAsnValThrSerPheAsnLeuArgGl 234

1165 ............................CTGAATAATGGAGAAAAT.... 1182
                                 :::|||::::::::::|||
 234 uAspSerLysPheThrPheIleLysTyrValAsnSerAlaArgAsnGlyA 251

1183 ...................ATTTCCTTTATTGACGAAGGAAAAGGCGAA 1212
                         :::   |||   ::::::||||||
 251 spValArgGlyArgSerPheAlaGlyValIlePheAsnAlaLysGly... 266

1213 TTGATACTTACCAGCAACATCAATCAAGGTGCTGGAGGATTATATTTCCA 1262
       ||||||::::::::|||         |||:::
 267 ......LeuThrThrSerPheAsnValLysLysGlySerThrVal..... 279

1263 AGGAGATTTTACGGTCTCGCCTGAAAATAACGAAACTTGGCAAGGCGCGG 1312
       ||||||   ::::::|||:::::::::   :::   |||
 280 ....AspPheLysLeuLysProAsnSerGlyTyrAsnSerGln...LysA 294

1313 GCGTTCATATCAGTGAAGACAGTACCGTTACTTGGAAAGTAAACGGCGTG 1362
       :::   |||:::   :::|||:::::::::   :::   :::|||
 294 rgIleProIleGlnPheGlnSerAsnIleSerValSerGlyGlyGlyArg 310

1363 GCAAAC...GACCGCCTGTCCAAAATCGGCAAAGGCACGCTGCACGTTCA 1409
     :::|||   :::   |||:::::::::      |||   ::::::::::
 311 ValAsnIleAsnThrLeuAlaAsnLeuThrGlyGlyGlyValGluIleAr 327

1410 AGCCAAAGGGGAAAACCAAGGCTCGATCAGCGTGGGCGACGGT...ACAG 1456
     ::::              :::|||||:::|||:::|||||   |||:
 327 gSer..............SerSerIleAsnValSerAspGlySerThrL 339

1457 TCATTTTGGATCAGCAGGCAGACGATAAAGGCAAAAAACAAGCCTTTAGT 1506
     ::   :::      ||||||   |||:::::      :::      :::
 339 euSerMetThrAlaGlnAlaArgAspArgAsnAlaPheGluIleThrLys 355

1507 GAAATCGGCTTGGTCAGCGGCAGGGGTACGGTGCAACTG........... 1545
     ::::::   :::   :::::::::::::::::::::::
 356 AspLeuValIleAsnAlaSerAsnSerAsnLeuSerIleIleGlnGlnAs 372

1546 ............................AATGCCGATAATCAGTTCAACC 1567
                                 ||||||   |||
 372 nAspGlyPheAspAsnAsnGlnLysAlaAsnAlaIleAsn.......... 385

1568 CCGACAAACTCTATTTCGGCTTTCGCGGCGGACGTTTGGATTTAAACGGG 1617
       :::|||            ::::::||||||::::::   |||:::|||
 386 ..SerLysTyrAsnValThrIleGlnGlyGlyAsnValThrLeuGlyGly 401

1618 CATTCGCTTTCGTTCCACCGTATTCAAAATACCGATGAAGGGGCGATGAT 1667

 401 ................................................... 401

1668 TGTCAACCACAATCAAGACAAAGAATCCACCGTTACCATTACAGGCAATA 1717
                         :::::|||:::   ||||||||||||:::
 402 ..................GlnAsnSerSerSerThrIleThrGlySerV 412

1718 AAGATATTGCTACAACCGGCAAT..............AACAACAGCTTG 1752
       :::|||:::::::::::::|||              :::|||:::
 412 alAsnIleGlyAlaAsnAlaAsnValThrLeuGlnAlaHisAsnGlyAsn 428

1753 GATAGCAAAAAAGAAATTGCCTACAACGGTTGGTTTGGCGAGAAAGATAC 1802
     |||   :::|||:::::::::::::::                  ::
 429 AspArgAsnLysLysLeuThrPheGly.....................As 438

1803 GACCAAAACGAACGGGCGGCTCAACCTTGTTTACCAGCCCGCCGCAGAAG 1852
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 438 nValSerValGluGlyGluLeuArgLeuValGlyAlaSerAlaAsnIleA 455

1853 ACCGCACCCTGCTGCTTTCCGGCGGAACAAATTTAAACGGCAACATCACG 1902
     :::::::::|||   ::::::::::|||:::::::::::::         :::
 455 snAsnAsnLeuSerValLysSerGlyAlaLysPheLys.........Ala 468

1903 CAAACAAACGGCAAACTGTTTTTCAGCGGCAGACCAACACCGCACGCCTA 1952
     :::||||||   :::|||   :::::::|||      |||   ::::::
 469 GluThrAsnAspAsnLeuAsnIleThrGlyThrPheThrAsnAsnGlyTh 485

1953 CAATCATTTAAACGACCATTGGTCGCAAAAAGAGGGCATTCCTCGC...G 1999
       :::   ::::::              |||:::|||      :::   |
 485 rSerIleIleAsp............ValLysLysGlyAlaAlaLysLeuG 498

2000 GGGAAATCGTGTGGGACAACGACTGGATCAACCGCACATTTAAAGCGGAA 2049
     ||:::|||:::   |||::::::   :::|||   |||   :::|||:::
 498 lyAsnIleThrAsnAspGlyAsn...LeuAsnIleThrThrAsnAlaLys 513

2050 AACTTCCAAATTAAAGGCGGACAGGCGGTGGTTTCCCGCAATGTTGCCAA 2099
     |||            |||   ::::::|||::::::   |||:::::::
 514 Asn............GlyGlnLysSerValIleAsnGlyAsnIleThrAs 526

2100 AGTGAAAGGCGATTGGCATTTGAGCAATCACGCCCAA............G 2137
     :   ||||||      :::::::::|||:::::::::
 526 nAsnLysGlyAlaLeuAsnIleThrAsnAsnGlyAsnAspThrGluIleG 543

2138 CAGTTTTTGGTGTCGCACCGCATCAAAGCCACACAATCTGTACACGTTCG 2187
       :::   |||         :::::::::   ::::::         |||
 543 lnIleGlyGlyAsnIleSerGlnLysGluGlyAsnLeuThrIleSerSer 559

2188 GACTGGACGGGTCTGACAAATTGTGTCGAA...AAAACCATTACCGAC.. 2232
     |||      ::::::|||:::   :::|||   |||:::   ||||||
 560 AspLysIleAsnIleThrLysArgIleGluIleLysAlaGlyThrAspGl 576

2233 ..........GATAAAGTGATTGCTTCATTGACTAAGACCGACATCAGCG 2272
               |||:::   :::||||||   ::::::      |||:::
 576 nGlyAsnSerAspSerGlyValAlaSerAsnAlaAsnLeuThrIleLys. 592

2273 GCAATGTCGATCTTGCCGATCACGCTCATTTAAATCTCACAGGG...... 2316
       :::   :::|||            :::||||||::::::|||
 593 ..ThrLysGluLeuLysLeuThrGluAsnLeuAsnIleSerGlyPheAsp 608

2317 ............CTTGCCACACTCAACGGCAATCTT.........AGTGC 2345
                 :::|||      |||:::||||||         :::
 609 LysAlaGluIleValAlaLysGluAsnAsnAsnLeuIleIleGlyAsnAs 625

2346 AAATGGCGAT......ACACGTTATACAGTCAGCCACAACGCCACCCAAA 2389
       |||||||||      :::      ||||||:::   |||   :::::::
 625 nAsnGlyAspAsnAlaAsnAlaLysThrValThrPheAsnAsnValLysA 642

2390 ACGGCAACCTTAGCCTCGTGGGCAATGCCCAAGCAACATTTAATCAA... 2436
     ::::::::::|||      |||:::   ::::::|||:::|||:::
 642 spSerLysIleSerAlaAsnGlyHis...AsnValThrLeuAsnSerLys 657

2437 ...GCCACATTAAACGGCAACACATCGGCTTCGGGCAATGCTTCATTTAA 2483
          |||   :::||||||:::::::::::|||||||::::::   ||
 658 ValGluThrSerAspGlyAsnSerAsnThrGluGlyAsnSerAspAsnAs 674

2484 T.........................................CTAA 2488
     |                                         ::::
 674 nAlaGlyLeuThrIleAspAlaLysAsnValThrValAsnAsnAspIleT 691

2489 GCGACCACGCCGTACAAAACGGCAGTCTGACGCTTTCCGGCAACGCTAAG 2538
     ::::::|||   :::   |||   :::   :::         ::::::|||
 691 hrSerHisLysThrValAsnIleThrAlaSerGluArgIleAspThrLys 707

2539 GCAAACGTAAGCCATTCCGCACTCAACGGTAATGTCTCCCTA........ 2580
     |||::::::::::   :::|||   :::||||||||||:::|||
 708 AlaAspThrThrIleAsnAlaThrThrGlyAsnValLysLeuThrAlaVa 724

2581 ............................GCCGATAAGGCAGTATTCCATT 2602
                                 :::::::::::::      ::::
 724 lThrSerAspIleGlnGlyGlyIleLysSerAsnSerGlyAspValAsnI 741
```

```
2603 TTGAAAGCAGCCGCTTTACCGGACAAATCAGCGGC.........GGCAAG 2643
     ::   :::|||      ||||||:::|||:::|||       :::|||
 741 leThrThrSer......ThrGlySerIleAsnGlyLysIleGluSerLys 755

2644 GATACGGCATTACACTTAAAAGACAGCGAATGGACGCTGCCGTCAGGCAC 2693
     :::   ::::::   |||      :::|||   ||||||
 756 SerGlySerValThrLeuThrAlaThrGluLysThrLeu........... 768

2694 GGAATTAGGCAATTTAAACCTTGACAACGCCACCATTACACTCAATTCCG 2743
       :::||||||::::::   :::::::::|||:::|||   |||   :
 769 .ThrValGlyAsnValSerGlyAsnThrValThrValThrAlaAsnArgG 785

2744 CCTATCGCCACGATGCGGCAGGGGCGCAAACCGGCAGTGCGACAGATGCG 2793
     ::               ||||||:::   |||   :::::::|||::::::
 785 lyAlaLeuThrThrLeuAlaGlySer...ThrIleAsnGlyThrAsnGly 800

2794 CCGCGCCGCCGTTCGCGCCGTTCGCGCCGTTCCCTATTATCCGTTACACC 2843
                ||||:::   ::::::   :::          :::
 801 ValThrThrSerSerGlnSerGlyGluIleGlyGlyGluValThrGlyLy 817

2844 GCCAACTTCGGTAGAATCCCGTTTCAACACGCTGACGGTAAACGGC.... 2889
       :::||||||   :::      ::::::||||||||||:::|||
 817 sThrValSerValThrAlaThrAlaGlySerLeuThrValLysGlyGlyA 834

2890 ..AAATTGAACGGT...CAGGGAACATTCCGCTTTATGTCGGAACTCTTC 2934
       |||:::|||:::   :::||||||      :::   ::::::
 834 laLysIleAsnAlaThrGluGlyThrAlaThrLeuThrAlaSer...... 848

2935 GGCTACCGCAGCGACAAATTGAAGCTGGCGGAAAGTTCCGAAGGCACT.. 2982
               |||   ||||||            |||||||:::   |||
 849 .........SerGlyLysLeuThrThrGluAlaSerSerAsnIleThrSe 862

2982 ..................................................... 2982

 862 rAlaLysGlyGlnValAspLeuSerAlaGlnAspGlySerIleAlaGlyG 879

2983 ...........TACACCTTGGCGGTCAACAATACCGGCAACGAACCTGCA 3021
                 :::::::::::::|||:::||||||:::
 879 lnIleSerAlaAlaAsnValThrLeuAsnThrThrGlyThr......... 892

3022 AGCCTCGAACAATTGACGGTAGTGGAAGGAAAAGACAACAAACCGGCTGTC 3071
               ||||||:::|||||||||  ::::::   |||
 893 ............LeuThrThrValGluGly.SerSerIleAsnAlaAsnG 905

3072 CGAAAACCTTAATTTCACCCTGC.....................AAAACG 3100
       ||||||:::      :::                        |||:::
 905 luGlyThrLeuValIleAsnAlaAsnAspAlaLysLeuAspGlyLysAla 921

3101 AACACGTCGATGCCGGCGCGTGGCGTTACCAACTCATCC.......... 3139
     :::   :::            ::::::||||||:::|||
 922 SerGlyAsnArgThrGluValAsnAlaThrAsnAlaSerGlySerGlySe 938

3140 .......GCAAAGACGGCGAGTTCCGCCTGCATAATCCGGTCAAAGAACA 3182
           ||||||||||:::||||||:::   |||      :::   |||
 938 rValThrAlaLysThrSerSerSerValAsnIleThrGlyAspLeuAsnT 955

3183 AGAGCTTTCCGACAAACTCGGCAAGGCAGAAGCCAAAAAACAGGCGGAAA 3232
                 |||         ::::::   :::|||      :::
 955 hrIleAsnGlyLeuAsnIleIleSerGluAsnGlyArgAsnThrValArg 971

3233 AAGACAACGCGCAAAGCCTTGACGCGCTGATTGCGGCCGGGCGCGAT... 3279
           ::::::      ::::::   ::::::||||||:::
 972 LeuArgGlyLysGluIleGluValLysTyrIleGlnProGlyValAlaSe 988

3280 ..........................GCCGTCGAAAAGACAGAAAGCG 3301
                                ::::::||||||::::::::::
 988 rValGluGluValIleGluAlaLysArgValLeuGluLysValLysAspL 1005

3302 TTGCCGAACCGGCCCGGCAGGCAGGCGGGGAAAATGTCGGCATTATGCAG 3351
     ::::::::      |||::::::   ::::::   :::|||:::
1005 euSerAspGluGluArgGluThrLeuAlaLys...LeuGlyValSerAla 1020

3352 GCGGAGGAAGAGAAAAAACGGGTGCAGGCGGATAAAGACACCGCCTTGGC 3401
     :::                ::::   ::::::   ::::::      ::::::
1021 Val.............ArgPheIleGluProAsnAsnThrIleThrValAs 1033

3402 GAAACAGCGCGAAGCGGAAACCCGGCCGGCTACC 3435
           |||:::|||      |||||||||::::::
1033 nThrGlnAsnGluPheThrThrArgProSerSer 1044
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seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2000.DAT:AAB01836

seq_documentation_block:

ID AAB01836 standard; Protein; 1079 AA.
XX
AC AAB01836;
XX
DT 11-SEP-2000 (first entry)
XX
DE Haemophilus influenzae strain LCDC2 HMW2A protein, SEQ ID NO:47.
XX
KW HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW recombinant production; Escherichia coli; antibacterial; vaccine;
KW human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW detection; diagnosis.
XX
OS Haemophilus influenzae strain LCDC2.
XX
PN WO200020609-A2.
XX
PD 13-APR-2000.
XX
PF 07-OCT-1999; 99WO-CA00938.
XX
PR 07-OCT-1998; 98US-0167568.
PR 08-DEC-1998; 98US-0206942.
XX
PA (CONN-) CONNAUGHT LAB LTD.
XX
PI Loosmore SM, Yang Y, Klein MH;
XX
DR WPI; 2000-303789/26.
DR N-PSDB; AAA52185.
XX
PT Nucleic acid molecule for producing recombinant high molecular weight
PT proteins of Haemophilus which are used as a vaccine to provide
PT protection against Haemophilus induced diseases in humans -
XX
PS Claim 12; Fig 23A-P; 307pp; English.
XX
CC The invention relates to the recombinant production of Haemophilus
CC influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC expression construct used to effect recombinant expression comprises a
CC promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC and the hmwB and hmwC genes encode accessory proteins which are
CC responsible for post-translational processing and secretion of the HMWA
CC proteins. The modified hmwABC operon used in the expression construct of
CC the invention contains an A gene modified such that it encodes only the
CC mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC vectors are used for the production of recombinant H. influenzae HMW
CC proteins which can be used as vaccines to mediate a humoral or
CC cell-mediated immune response to provide protection against diseases in
CC humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC antigens in immunoassays for detecting antibodies against Haemophilus,
CC HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC HMW proteins can be used to isolate and clone hmw genes from other
CC non-typeable strains of Haemophilus via hybridisation reactions. The

CC present sequence represents an HMWA protein from a non-typeable strain of
CC H. influenzae.
XX
SQ Sequence 1079 AA;

alignment_scores:
Quality: 268.00 Length: 1062
Ratio: 0.485 Gaps: 53
Percent Similarity: 52.072 Percent Identity: 20.716

alignment_block:
US-09-303-518D-649 x AAB01836 ..

Align seg 1/1 to: AAB01836 from: 1 to: 1079

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 787 TCATTTGGCGACAGTGGCTCACCAATGTTTATCTATGATGCCCAAAAGCA 836
  78 AsnIleGlyAspSerGlyHis...LeuThrLeuTyrLysLysArgLysAs 93

 837 AAAGTGGTTAATTAATGGGGTATTGCAAACGGGCAACCCCTATATAGGAA 886
  93 nArg.........SerAspGlyIleGlnIleAsnLysAspIleThrSerT 107

 887 AAAGCAATGGCTTCCAGCTGGTTCGTAAAGATTGG......TTCTATGAT 930
 107 hrGlyGlySerLeuThrIleAsnSerAspAspTrpValAspIleHisGly 123

 931 GAAATCTTTGCTGGAGAT.....................ACCCATTCAGT 959
 124 AsnIleThrLeuGlyGluGlyPheLeuAsnIleThrSerSerAspSerVa 140

 960 ATTCTACGAA..................................... 969
 140 lAlaPheGluGlyGlyAsnGlyAsnLysGlyArgSerSerAlaSerAlaG 157

 970 ..........................CCACGTCAAAATGGGAAATAC 990
 157 lnIleIleAlaGlnGlyThrIleThrLeuThrGlyGluAsnLysThrPhe 173

 991 TCTTTTAACGACGATAAT...AATGGCACAGGAAAA...ATCAATGCCAA 1034
 174 ArgLeuAsnAsnValSerLeuAsnGlyThrGlyAsnGlyLeuSerIleIl 190

1035 ACATGAACACAATTCTCTGCCTAATAGATTAAAAACACGAACCGTTCAAT 1084
 190 eSerThrAlaSerAsnLeuSerHisArgLeuAspGlyGluIleAsnValS 207

1085 TGTTTAATGTTTCTTTATCCGAGACAGCAAGAGAACCTGTT...TATCAT 1131
 207 erGlyAsnValThrIleAsnGlnThrThrGlnGlnAsnIleGluTyrTrp 223

1132 GCTGCAGGT..............GGTGTCAACAGTTATCGACCCAGA.. 1164
 224 LysAlaSerSerAspSerTyrTrpAsnValThrSerPheAsnLeuArgGl 240

1165 ..........................CTGAATAATGGAGAAAAT.... 1182
 240 uAspSerLysPheThrPheIleLysTyrValAsnSerAlaArgAsnGlyA 257

1183 ....................ATTTCCTTTATTGACGAAGGAAAAGGCGAA 1212
 257 spValArgGlyArgSerPheAlaGlyValIlePheAsnAlaLysGly... 272

1213 TTGATACTTACCAGCAACATCAATCAAGGTGCTGGAGGATTATATTTCCA 1262
 273 ......LeuThrThrSerPheAsnValLysLysGlySerThrVal..... 285

1263 AGGAGATTTTACGGTCTCGCCTGAAAATAACGAAACTTGGCAAGGCGCGG 1312
 286 ....AspPheLysLeuLysProAsnSerGlyTyrAsnSerGln...LysA 300

1313 GCGTTCATATCAGTGAAGACAGTACCGTTACTTGGAAAGTAAACGGCGTG 1362

 300 rgIleProIleGlnPheGlnSerAsnIleSerValSerGlyGlyGlyArg 316

1363 GCAAAC...GACCGCCTGTCCAAAATCGGCAAAGGCACGCTGCACGTTCA 1409
 317 ValAsnIleAsnThrLeuAlaAsnLeuThrGlyGlyGlyValGluIleAr 333

1410 AGCCAAAGGGGAAAACCAAGGCTCGATCAGCGTGGGCGACGGT...ACAG 1456
 333 gSer.............SerSerIleAsnValSerAspGlySerThrL 345

1457 TCATTTTGGATCAGCAGGCAGACGATAAAGGCAAAAAACAAGCCTTTAGT 1506
 345 euSerMetThrAlaGlnAlaArgAspArgAsnAlaPheGluIleThrLys 361

1507 GAAATCGGCTTGGTCAGCGGCAGGGGTACGGTGCAACTG.......... 1545
 362 AspLeuValIleAsnAlaSerAsnSerAsnLeuSerIleIleGlnGlnAs 378

1546 ..........................AATGCCGATAATCAGTTCAACC 1567
 378 nAspGlyPheAspAsnAsnGlnLysAlaAsnAlaIleAsn.......... 391

1568 CCGACAAACTCTATTTCGGCTTTCGCGGCGGACGTTTGGATTTAAACGGG 1617
 392 ..SerLysTyrAsnValThrIleGlnGlyGlyAsnValThrLeuGlyGly 407

1618 CATTCGCTTTCGTTCCACCGTATTCAAAATACCGATGAAGGGGCGATGAT 1667

 407 ..... 407

1668 TGTCAACCACAATCAAGACAAAGAATCCACCGTTACCATTACAGGCAATA 1717
 408 ..................GlnAsnSerSerSerThrIleThrGlySerV 418

1718 AAGATATTGCTACAACCGGCAAT..............AACAACAGCTTG 1752
 418 alAsnIleGlyAlaAsnAlaAsnValThrLeuGlnAlaHisAsnGlyAsn 434

1753 GATAGCAAAAAAGAAATTGCCTACAACGGTTGGTTTGGCGAGAAAGATAC 1802
 435 AspArgAsnLysLysLeuThrPheGly.....................As 444

1803 GACCAAAACGAACGGGCGGCTCAACCTTGTTTACCAGCCCGCCGCAGAAG 1852
 444 nValSerValGluGlyGluLeuArgLeuValGlyAlaSerAlaAsnIleA 461

1853 ACCGCACCCTGCTGCTTTCCGGCGGAACAAATTTAAACGGCAACATCACG 1902
 461 snAsnAsnLeuSerValLysSerGlyAlaLysPheLys.........Ala 474

1903 CAAACAAACGGCAAACTGTTTTTCAGCGGCAGACCAACACCGCACGCCTA 1952
 475 GluThrAsnAspAsnLeuAsnIleThrGlyThrPheThrAsnAsnGlyTh 491

1953 CAATCATTTAAACGACCATTGGTCGCAAAAAGAGGGCATTCCTCGC...G 1999
 491 rSerIleIleAsp............ValLysLysGlyAlaAlaLysLeuG 504

2000 GGGAAATCGTGTGGGACAACGACTGGATCAACCGCACATTTAAAGCGGAA 2049
 504 lyAsnIleThrAsnAspGlyAsn...LeuAsnIleThrThrAsnAlaLys 519

2050 AACTTCCAAATTAAAGGCGGACAGGCGGTGGTTTCCCGCAATGTTGCCAA 2099
 520 Asn............GlyGlnLysSerValIleAsnGlyAsnIleThrAs 532

2100 AGTGAAAGGCGATTGGCATTTGAGCAATCACGCCCAA............G 2137
 532 nAsnLysGlyAlaLeuAsnIleThrAsnAsnGlyAsnAspThrGluIleG 549

2138 CAGTTTTTGGTGTCGCACCGCATCAAAGCCACACAATCTGTACACGTTCG 2187
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 549 lnIleGlyGlyAsnIleSerGlnLysGluGlyAsnLeuThrIleSerSer 565

2188 GACTGGACGGGTCTGACAAATTGTGTCGAA...AAAACCATTACCGAC.. 2232
     |||      ::::::|||:::   :::|||   |||:::   ||||||
 566 AspLysIleAsnIleThrLysArgIleGluIleLysAlaGlyThrAspGl 582

2233 .........GATAAAGTGATTGCTTCATTGACTAAGACCGACATCAGCG 2272
             |||:::   :::|||||||   ::::::      |||:::
 582 nGlyAsnSerAspSerGlyValAlaSerAsnAlaAsnLeuThrIleLys. 598

2273 GCAATGTCGATCTTGCCGATCACGCTCATTTAAATCTCACAGGG...... 2316
       :::   :::|||            :::||||||:::::|||
 599 ..ThrLysGluLeuLysLeuThrGluAsnLeuAsnIleSerGlyPheAsp 614

2317 ............CTTGCCACACTCAACGGCAATCTT.........AGTGC 2345
                 :::|||    |||:::||||||        :::
 615 LysAlaGluIleValAlaLysGluAsnAsnAsnLeuIleIleGlyAsnAs 631

2346 AAATGGCGAT......ACACGTTATACAGTCAGCCACAACGCCACCCAAA 2389
      |||||||||      :::      ||||||:::   |||   :::::::
 631 nAsnGlyAspAsnAlaAsnAlaLysThrValThrPheAsnAsnValLysA 648

2390 ACGGCAACCTTAGCCTCGTGGGCAATGCCCAAGCAACATTTAATCAA... 2436
     ::::::::::|||      |||:::   :::::::|||:::|||:::
 648 spSerLysIleSerAlaAsnGlyHis...AsnValThrLeuAsnSerLys 663

2437 ...GCCACATTAAACGGCAACACATCGGCTTCGGGCAATGCTTCATTTAA 2483
        |||   :::|||||:::::::::::::|||||:::::   ||
 664 ValGluThrSerAspGlyAsnSerAsnThrGluGlyAsnSerAspAsnAs 680

2484 T.........................................CTAA 2488
     |                                        :::
 680 nAlaGlyLeuThrIleAspAlaLysAsnValThrValAsnAsnAspIleT 697

2489 GCGACCACGCCGTACAAAACGGCAGTCTGACGCTTTCCGGCAACGCTAAG 2538
     :::::|||   :::   |||   :::   :::         :::::|||
 697 hrSerHisLysThrValAsnIleThrAlaSerGluArgIleAspThrLys 713

2539 GCAAACGTAAGCCATTCCGCACTCAACGGTAATGTCTCCCTA........ 2580
     |||:::::::::   :::|||   :::||||||||||:::|||
 714 AlaAspThrThrIleAsnAlaThrThrGlyAsnValLysLeuThrAlaVa 730

2581 ............................GCCGATAAGGCAGTATTCCATT 2602
                                :::::::::::      ::::
 730 lThrSerAspIleGlnGlyGlyIleLysSerAsnSerGlyAspValAsnI 747

2603 TTGAAAGCAGCCGCTTTACCGGACAAATCAGCGGC.........GGCAAG 2643
     ::   :::|||      ||||||:::|||:::|||        :::|||
 747 leThrThrSer......ThrGlySerIleAsnGlyLysIleGluSerLys 761

2644 GATACGGCATTACACTTAAAAGACAGCGAATGGACGCTGCCGTCAGGCAC 2693
     :::   ::::::   |||      :::|||   ||||||
 762 SerGlySerValThrLeuThrAlaThrGluLysThrLeu........... 774

2694 GGAATTAGGCAATTTAAACCTTGACAACGCCACCATTACACTCAATTCCG 2743
         :::||||||::::::   :::::::::|||:::|||   |||   :
 775 .ThrValGlyAsnValSerGlyAsnThrValThrValThrAlaAsnArgG 791

2744 CCTATCGCCACGATGCGGCAGGGGCGCAAACCGGCAGTGCGACAGATGCG 2793
     ::                |||||||:::   |||   :::::::|||:::::
 791 lyAlaLeuThrThrLeuAlaGlySer...ThrIleAsnGlyThrAsnGly 806

2794 CCGCGCCGCCGTTCGCGCCGTTCGCGCCGTTCCCTATTATCCGTTACACC 2843
                |||:::   ::::::   :::         :::
 807 ValThrThrSerSerGlnSerGlyGluIleGlyGlyGluValThrGlyLy 823

2844 GCCAACTTCGGTAGAATCCCGTTTCAACACGCTGACGGTAAACGGC.... 2889
         :::||||||   :::      ::::::||||||||||:::|||
 823 sThrValSerValThrAlaThrAlaGlySerLeuThrValLysGlyGlyA 840

2890 ..AAATTGAACGGT...CAGGGAACATTCCGCTTTATGTCGGAACTCTTC 2934
       |||:::|||:::   :::||||||      :::   ::::::
 840 laLysIleAsnAlaThrGluGlyThrAlaThrLeuThrAlaSer...... 854

2935 GGCTACCGCAGCGACAAATTGAAGCTGGCGGAAAGTTCCGAAGGCACT.. 2982
              |||   ||||||            ||||||:::   |||
 855 .........SerGlyLysLeuThrThrGluAlaSerSerAsnIleThrSe 868

2982 ................................................. 2982

 868 rAlaLysGlyGlnValAspLeuSerAlaGlnAspGlySerIleAlaGlyG 885

2983 ...........TACACCTTGGCGGTCAACAATACCGGCAACGAACCTGCA 3021
                        :::::::::::|||:::||||||:::
 885 lnIleSerAlaAlaAsnValThrLeuAsnThrThrGlyThr......... 898

3022 AGCCTCGAACAATTGACGGTAGTGGAAGGAAAAGACAACAAACCGCTGTC 3071
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 899 ............LeuThrThrValGluGly.SerSerIleAsnAlaAsnG 911

3072 CGAAAACCTTAATTTCACCCTGC.....................AAAACG 3100
           ||||||:::      :::                    |||:::
 911 luGlyThrLeuValIleAsnAlaAsnAspAlaLysLeuAspGlyLysAla 927

3101 AACACGTCGATGCCGGCGCGTGGCGTTACCAACTCATCC........... 3139
     :::   :::             ::::::||||||:::|||
 928 SerGlyAsnArgThrGluValAsnAlaThrAsnAlaSerGlySerGlySe 944

3140 .......GCAAAGACGGCGAGTTCCGCCTGCATAATCCGGTCAAAGAACA 3182
            |||||||||:::||||||:::   |||      :::   |||
 944 rValThrAlaLysThrSerSerSerValAsnIleThrGlyAspLeuAsnT 961

3183 AGAGCTTTCCGACAAACTCGGCAAGGCAGAAGCCAAAAAACAGGCGGAAA 3232
                  |||         ::::::   :::|||      :::
 961 hrIleAsnGlyLeuAsnIleIleSerGluAsnGlyArgAsnThrValArg 977

3233 AAGACAACGCGCAAAGCCTTGACGCGCTGATTGCGGCCGGGCGCGAT... 3279
               ::::::      ::::::   ::::::||||||:::
 978 LeuArgGlyLysGluIleGluValLysTyrIleGlnProGlyValAlaSe 994

3280 ............................GCCGTCGAAAAGACAGAAAGCG 3301
                                ::::::||||||::::::::::
 994 rValGluGluValIleGluAlaLysArgValLeuGluLysValLysAspL 1011

3302 TTGCCGAACCGGCCCGGCAGGCAGGCGGGGAAAATGTCGGCATTATGCAG 3351
     :::::::      |||::::::   ::::::   :::|||:::
1011 euSerAspGluGluArgGluThrLeuAlaLys...LeuGlyValSerAla 1026

3352 GCGGAGGAAGAGAAAAAACGGGTGCAGGCGGATAAAGACACCGCCTTGGC 3401
     :::             :::   ::::::   ::::::      ::::::
1027 Val............ArgPheIleGluProAsnAsnThrIleThrValAs 1039

3402 GAAACAGCGCGAAGCGGAAACCCGGCCGGCTACC 3435
        |||:::|||      |||||||||::::::
1039 nThrGlnAsnGluPheThrThrArgProSerSer 1050
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seq_documentation_block:
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AC   AAR41725;
XX
DT   26-APR-1994  (first entry)
XX
DE   High molecular weight protein 1 (HMW1).
XX
KW   HMW; high molecular weight protein; virus; vaccine; influenza;
KW   epitope; immunity; haemophilus influenzae; gene cluster.
XX
OS   Haemophilus influenzae.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 668..677
FT                   /note= "Possibly incorrect sequence. Alternative
FT                         sequence for this region is LNVSESGEFN.
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FT                              (See comments)."
XX
PN   WO9319090-A.
XX
PD   30-SEP-1993.
XX
PF   16-MAR-1993;   93WO-US02166.
XX
PR   16-MAR-1992;   92GB-0005704.
XX
PA   (BARE/) BARENKAMP S J.
PA   (INRM ) INSERM INST NAT SANTE & RECH MEDICALE.
XX
PI   Barenkamp SJ;
XX
DR   WPI; 1993-320683/40.
DR   N-PSDB; AAQ49508.
XX
PT   High molecular weight surface proteins - of non-typeable
PT   haemophilus which exhibit immunogenic properties
XX
PS   Claim 3; Figure 2/10; 100pp; English.
XX
CC   The isolation and purification of the high molecular weight protein
CC   enables the identification of the major protective epitopes of the
CC   protein by conventional epitope mapping.  These epitopes can then be
CC   synthesised using standard techniques and incorporated into fully
CC   synthetic or recombinant vaccines.  This sequence is claimed to be
CC   the same as that given in AAR41723 (High molecular weight protein 1)
CC   although it does differ slightly. (Repeated regions which are
CC   possibly incorrect and occur in the corresponding nucleotide coding
CC   sequence contribute to these differences).
XX
SQ   Sequence   1536 AA;


alignment_scores:
           Quality:  267.50              Length:   1173
             Ratio:  0.444                Gaps:     58
 Percent Similarity:  51.407   Percent Identity: 21.057

alignment_block:
 US-09-303-518D-649 x AAR41725   ..

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     127 GGACACACTTATTTCGGCATCAACTACCAATACTATCGCGACTTTGCCGA 176
         |||:::|||||::::|||                              :::::
     349 GlyGluThrTyrLeuGly.........................GlyAs 356

     177 AAATAAAGGCAAGTTTGCAGTCGGGGCGAAAGATATTGAGGTTTACAACA 226
         :::::::|||:::          |||   :::   |||::::::   :::|
     356 pGluArgGlyGlu.........GlyLysAsnGlyIleGlnLeuAlaLysL 370

     227 AAAAAGGGGAGTTGGTCGGCAAATCAATGACAAAAGCCCCGATGATTGAT 276
         ||                    |||:::   |||:::      |||:::
     370 ys.................ThrSerLeuGluLysGlySerThrIleAsn 380

     277 TTTTCTGTGGTGTCGCGTAACGGCGTGGCGGCATTGGTGGGCGATCAATA 326
           |||      :::::::::|||   |||   :::   ||||||
     381 ValSerGlyLysGluLysGlyGlyArgAlaIleValTrpGlyAspIleAl 397

     327 TATTGTG..............................AGCGTGGCACATA 346
          ::::::                             ::::::|||   :
     397 aLeuIleAspGlyAsnIleAsnAlaGlnGlySerGlyAspIleAlaLysT 414

     347 ACGGCGGCTAT..................................... 357
         ::|||||:::
     414 hrGlyGlyPheValGluThrSerGlyHisAspLeuPheIleLysAspAsn 430

     358 ..................................AACAACGTTGATTT 371
                                          :::|||||:::::
     431 AlaIleValAspAlaLysGluTrpLeuLeuAspProAspAsnValSerIl 447

     372 TGGTGCGGAA......GGAAGAAATCCCGATCAACATCGTTTTACTTAT. 414
         ::::|||||      ||||||:::      ::::::         |||
     447 eAsnAlaGluThrAlaGlyArgSerAsnThrSerGluAspAspGluTyrT 464

     415 ....................AAAATTGTGAAACGGAATAATTATAAAGCA 444
                              :::      |||||||||:::   |||:::
     464 hrGlySerGlyAsnSerAlaSerThrProLysArgAsnLysGluLysThr 480

     445 GGGACTAAAGGCCATCCTTATGGCGGCGATTATCATATGCCGCGTTTGCA 494
             |||            :::   :::|||:::      :::    :
     481 .ThrLeuThrAsnThrThrLeuGluSerIleLeuLysLysGlyThrPheV 497

     495 TAAATTTGTCACAGATGCAGAACCTGTTGAAATGACCAGTTATATGGATG 544
         ::|||::::::      |||:::                  |||::::::
     497 alAsnIleThrAlaAsnGlnArg.................IleTyrVal 507

     545 GGCGGAAATATATCGATCAAAATAATTACCCTGACCGTGTTCGTATTGGG 594
         :::::::::|||:::::::::      :::||||||::::::      ||
     508 AsnSerSerIleAsnLeuSerAsnGlySerLeuThrLeuTrpSerGluGl 524

     595 GCAGGCAGGC..........................AATATTGGCGATC 617
         |:::::::|||                          :::   ||||||
     524 yArgSerGlyGlyGlyValGluIleAsnAsnAspIleThrThrGlyAspA 541

     618 TGATGAAGATGAGCCCAATAACC..................GCGAAAGTT 649
             :::   :::   :::|||                   :::   |||
     541 spThrArgGlyAlaAsnLeuThrIleTyrSerGlyGlyTrpValAspVal 557

     650 CATATCATATTGCAAGTGCGTATTCTTGGCTCGTTGGTGGCAATACCTTT 699
         |||      :::::::::         |||::::::  :::   |||
     558 HisLysAsnIleSerLeuGlyAlaGlnGlyAsnIle..AsnIleThrAla 573

     700 GCACAAAAT..............GGATCA..............GGTGG 719
             |||:::              ||||||               |||
     574 LysGlnAspIleAlaPheGluLysGlySerAsnGlnValIleThrGlyGl 590

     720 TGGCACAGTCAACTTAGGTAGTGAAAAAATTAAACATAGCCCATATGGTT 769
          ||||||::::::   |||::::::|||                  ||||
     590 nGlyThrIleThrSerGlyAsnGlnLys.................GlyP 601

     770 TTTTACCAACAGGAGGCTCATTTGGCGACAGTGGCTCACCAATGTTTATC 819
         ||       ::::::   |||::::::   :::||||||   :::   :::
     601 heArgPheAsnAsnValSerLeuAsnGlyThrGlySerGlyLeuGlnPhe 617

     820 TATGATGCCCAAAAGCAAAAGTGGTTAATTAATGGGGTATTGCAAACGGG 869
                 :::   :::|||:::   |||::::::   ::::::
     618 ThrThrLysArgThrAsnLysTyrAlaIleThrAsnLysPheGluGlyTh 634

     870 CAACCCCTATATAGGAAAAAGCAAT...GGCTTCCAGCTGGTTCGTAAAG 916
                    ||||||   |||   ::::::   |||   :::::::
     634 rLeuAsnIleSerGlyLysValAsnIleSerMetValLeuProLysAsnG 651

     917 ATTGGTTCTATGATGAAATCTTTGCTGGAGATACCCATTCAGTATTCTAC 966
         ::      ||||||:::   |||   |||   |||:::      :::
     651 luSerGlyTyrAspLys...PheLysGlyArgThrTyrTrpAsnLeuThr 666

     967 GAACCACGTCAA......AATGGGAAATACTCTTTTAACGACGATAATAA 1010
         :::      :::      |||:::|||   :::::::::   |||:::::
     667 SerLysValAspMetIleAsnSerLysAspAlaLeuThrIleAspSerAr 683

    1011 TGGCACA.........GGAAAAATCAATGCCAAACATGAACACAATTCTC 1051
         :|||:::         |||   ::::::      ::::::   |||::::
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1249 GGATTATATTTCCAAGGAGATTTTACGGTCTCGCCTGAAAATAACGAAAC 1298
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760 l...GlnThrProGlyValValIleAsnSerLysTyrPheAsnValSerT 776
1328 AAGACAGTACCGTTACTTGGAAAGTAAACGGC..... 1359
776 hrGlySerSerLeuArgPheLysThrSerGlySerThrLysThrGlyPhe 792
1360 ...GTGGCAAACGAC...CGCCTGTCCAAAATCGGCAAAGGCACGCTGCA 1403
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1404 CGTTCAAGCCAAAGGGGAAAACCAAGGCTCGATCAGCGTGGGCGACGGTA 1453
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1454 CAGTCATTTTGGATCAGCAGGCAGACGATAAAGGCAAAAAACAAGCCTTT 1503
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1504 AGTGAAATCGGCTTGGTCAGCGGCAGGGGTACGGTGCAACTGAATGCCGA 1553
840 SerArgLysAlaValThrGluIleGluGlyAsnValThrIleAsn..... 854
1554 TAATCAGTTCAACCCCGACAAACTCTATTTCGGCTTTCGCGGCGGACGTT 1603
855 .....AsnAsnAlaAsnV 859
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859 alThrLeuIleGlySerAspPheAspAsnHisGlnLysProLeuThrIle 875
1654 GAAGGGGCGATGATTGTCAACCACAATCAA......GACAAAGAATCCAC 1697
876 LysLysAspValIleIleAsnSerGlyAsnLeuThrAlaGlyGlyAsnIl 892
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1741 .....AACAACAGCTTG 1752
909 laIleThrAsnPheThrPheAsnValGlyGlyLeuPheAspAsnLysGly 925
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1008 GlnIleThrIleLysAlaGly.....ValAspGl 1017
2100 AGTGAAAGGCGATTGGCATTTGAGCAATCACGCCCAAGCAGTTTTTGGTG 2149
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2150 TCGCACCGCATCAAAGCCACACAATCTGTACACGTTCGGACTGGACGGGT 2199
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     1237 leSerGly...GlyThrValGluValLysAlaThrGluSerLeuThrThr 1252

     2938 TACCGCAGCGACAAATTGAAGCTGGCGGAAAGTTCCGAAGGCACTTACAC 2987
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     2988 CTTGGCGGTC.....................AACAATACCGGCAACG 3013
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     1268 rSerAlaThrGlyThrIleGlyGlyThrIleSerGlyAsnThrValAsnV 1285

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     3043 ...GTGGAAGGAAAAGACAACAAACCGCTGTCCGAAAACCTTAATTTCAC 3089
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     1302 AlaThrGluGlyAlaAlaThrLeuThrThrSerSerGlyLysLeuThrTh 1318

     3090 CCTGCAAAACGAACACGTCGATGCCGGCGCGTGGCGTTACCAACTCATCC 3139
          |      ::::::|||:::   ::: |||:::|||   :::|||   |||
     1318 rGluAlaSerSerHisIleThrSer.AlaLysGlyGlnValAsnLeuSer 1334

     3140 GCAAAGACGGCGAGTTCCGCCTGCATAATCCGGTCAAAGAACAAGAGCTT 3189
          |||:::   :::|||   |||      |||::::::   |||   :::::
     1335 AlaGlnAspGlySerValAlaGlySerIleAsnAlaAlaAsnValThrLe 1351

     3190 TCCGACAAACTCGGCAAGGCAGAAGCCAAAAAACAGGCGGAAAAAGACAA 3239
          :   |||::::::::::           |||:::   :::   ::::::|
     1351 uAsnThrThrGlyThrLeuThrThrValLysGlySerAsnIleAsnAlaT 1368

     3240 CGCGCAAAGCCTTG 3253
          ||     :::|||
     1368 hrSerGlyThrLeu 1372
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seq_documentation_block:

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ID   AAB01825 standard; Protein; 1221 AA.
XX
AC   AAB01825;
XX
DT   11-SEP-2000  (first entry)
XX
DE   Haemophilus influenzae strain Joyc mature HMW1A protein, SEQ ID NO:28.
XX
KW   Mature HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW   non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW   recombinant production; Escherichia coli; antibacterial; vaccine;
KW   human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW   detection; diagnosis.
XX
OS   Haemophilus influenzae strain Joyc.
XX
PN   WO200020609-A2.
XX
PD   13-APR-2000.
XX
PF   07-OCT-1999;   99WO-CA00938.
XX
PR   07-OCT-1998;   98US-0167568.
PR   08-DEC-1998;   98US-0206942.
XX
PA   (CONN-) CONNAUGHT LAB LTD.
XX
PI   Loosmore SM,  Yang Y,  Klein MH;
XX
DR   WPI; 2000-303789/26.
DR   N-PSDB; AAA52176.
XX
PT   Nucleic acid molecule for producing recombinant high molecular weight
PT   proteins of Haemophilus which are used as a vaccine to provide
PT   protection against Haemophilus induced diseases in humans -
XX
PS   Claim 8; Fig 18A-R; 307pp; English.
XX
CC   The invention relates to the recombinant production of Haemophilus
CC   influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC   expression construct used to effect recombinant expression comprises a
CC   promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC   to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC   influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC   clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC   hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC   and the hmwB and hmwC genes encode accessory proteins which are
CC   responsible for post-translational processing and secretion of the HMWA
CC   proteins. The modified hmwABC operon used in the expression construct of
CC   the invention contains an A gene modified such that it encodes only the
CC   mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC   and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC   strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC   vectors are used for the production of recombinant H. influenzae HMW
CC   proteins which can be used as vaccines to mediate a humoral or
CC   cell-mediated immune response to provide protection against diseases in
CC   humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC   pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC   antigens in immunoassays for detecting antibodies against Haemophilus,
CC   HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC   HMW proteins can be used to isolate and clone hmw genes from other
CC   non-typeable strains of Haemophilus via hybridisation reactions. The
CC   present sequence represents a mature HMWA protein from a non-typeable
CC   strain of H. influenzae.
XX
SQ   Sequence   1221 AA;
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alignment_scores:

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            Quality:  265.00          .Length:    900
              Ratio:  0.559             Gaps:     48
 Percent Similarity:  52.667   Percent Identity: 21.222
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alignment_block:

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     146 ThrGlyGlnGlyThrIleThrAlaGlyAsnGlyLysGlyPheArgPheGl 162

     753 ACATAGCCCATATGGTTTTTTACCAACAGGAGGCTCATTTGGC....... 795
         :::::::      :::   :::   ||||||      |||:::
     162 uAsnAlaSerLeuAsnGlyIleGlyThrGlyLeuLeuPheAsnIleLysA 179

     796 ..GACAGTGGCTCACCAATGTTTATCTATGATGCCCAAAAGCAAAAGTGG 843
           |||   |||:::   :::   |||   :::
     179 rgAspLeuGlyAsnAsnPheGlnIleIleAsn.................. 189

     844 TTAATTAATGGGGTATTGCAAACGGGCAACCCCTATATAGGAAAAAGCAA 893
         ::::::||||||:::|||:::   :::            ||||||   ||
     190 PhePheAsnGlyThrLeuAsnIleSer.............GlyLysValAs 202

     894 TGGCTTCCAGCTGGTTCGTAAAGATTGGTTCTATGATGAAATCTTTGCTG 943
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     202 nIleSerMetValIleProLysLysTrpAspTyrSerLys...PheArgG 218

     944 GAGATACCCAT......TCAGTATTCTACGAACCACGTCAAAATGGGAAA 987
         ||   |||:::         :::      :::      :::::::::|||
     218 lyArgThrTyrTrpAsnValThrHisLeuAsnValSerGluGlySerLys 234

     988 TACTCTTTTAACGACGATAATAATGGC.........ACAGGAAAAATCAA 1028
         ::::::::::::   |||:::::::|||         :::|||   :::||
     235 PheAsnLeuThrIleAspSerArgGlyAspAspThrAlaGlyThrLeuAs 251
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1029 TGCCAAACATGAACACAATTCTCTGCCTAATAGATTAAAAACACGAACCG 1078
251 nThrProTyrAsnLeuAsnGlyIleSerPheAsnLysAspThr..... 265
1079 TTCAATTGTTTAATGTT.....TCTTTATCCGAGACAGCAAGA 1116
266 .....IlePheAspValLysGlnAsnGlyAlaValThrPheAspIleLys 280
1117 GAACCTGTTTATCATGCTGCAGGTGGTGTCAACAGTTATCGACCC..... 1161
281 AlaProIle.....GlyValAsnAsnAsnArgAsnLeuAs 292
1162 .....AGACTGAATAATGGAGAAAATATTT 1186
292 nTyrAlaSerPheAsnGlyAsnIleSerValSerGlyGlyGlyAsnValT 309
1187 CCTTT.....ATTGACGAAGGAAAAGGCGAATTG 1215
309 hrPheLysLeuLeuAlaSerSerSerThrAlaGlnThrProGlyValPhe 325
1216 ATACTTACCAGCAACATCAAT...CAAGGTGCTGGAGGATTATATTTCCA 1262
326 IleAsnSerLysHisPheAsnAlaSerGlyGlySerSerLeuGluPheAr 342
1263 AGGAGAT.....TTTACGGTCTCGCCTGAAAATAACG 1294
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357 euThrLeuAsnAlaThrGlyGlyAsnIleSer.....Leu 368
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369 LeuGlnValGluGlyIleAsp.....GlyMetIleGlyLysGl 381
1395 CACGCTGCACGTTCAAGCCAAAGGGGAAAACCAAGGCTCGATCAGCGTGG 1444
381 y.....ValValAlaLys.....LysAsnIleThrPheA 391
1445 GCGACGGTACAGTCATTTTGGATCAGCAGGCAGACGATAAAGGCAAAAAA 1494
391 laGlyGlyAsnIleThrPhe.....GlySerLys 400
1495 CAAGCCTTTAGTGAAATCGGCTTGGTCAGCGGCAGGGGTACGGTGCAACT 1544
401 LysAlaIleThrGluIle.....GluGlyAsnAlaThrIleAsnAs 414
1545 GAATGCC.....GATAATCAGTTCAACC 1567
414 nAsnAlaAsnValThrLeuIleGlySerAspPheAspAsnHisGlnLysP 431
1568 CC.....GACAAACTCTATTTCGGCTTTCGCGGCGGACGT 1602
431 roLeuThrIleLysLysAspValIle.....IleAsnSerGlyAsn 444
1603 TTGGATTTAAACGGGCATTCGCTTTCGTTCCACCGTATTCAAAATACCGA 1652
445 LeuThrAlaGlyGlyAsnValIleAsnIleAsn..... 455
1653 TGAAGGGGCGATGATTGTCAACCACAATCAAGACAAAGAATCCACCGTTA 1702
456 ....GlyAsnLeuThrValAsnAsnGlyAlaAsnLeuLysAlaIleThrA 471
1703 CCATTACAGGCAATAAAGATATTGCTACAACCGGCAAT.....AACAAC 1746
471 snPheThrPheAsn.....ValGlyGlyLeuPheAspAsn 482
1747 AGCTTGGATAGCAAAAAAGAAATTGCCTACAACGGTTGGTTTGGCGAGAA 1796
483 LysGlyAsnSerAsnIleSerIleAla...ArgGlyGlyAlaLysPheLy 498
1797 AGATACGACCAAAACGAACGGGCGGCTCAACCTTGTTTACCAGCCCGCCG 1846
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2407 ......GTGGGCAATGCCCAAGCAACATTTAATCAAGCCACATTAAACGG 2450
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2451 C.....AACACATCGGCTTCGGGCAATG 2473
731 yGlyIleGluSerAsnSerGlyAsnValAsnIleThrAlaSerGlyAsp. 747
2474 CTTCATTTAATCTAAGCGACCACGCCGTACAAAACGGCAGTCTGACGCTT 2523
748 ..ThrLeuAsnValSerAsnIleThrGlyGlnAsnValThrValAlaAla 763
2524 TCCGGCAACGCTAAGGCAAACGTAAGCCATTCCGCACTCAAC..... 2565
764 AlaSerGlyAlaValThrThrThrLysGlySerThrIleAsnAlaThrTh 780
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 780 rGlyAsnAlaAsnIleThrThrLys..................... 788

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2706 TTTAAACCTTGACAACGCCACCATTACACTCAATTCCGCCTATCGCCACG 2755
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2853 GGTAGAATCCCGTTTCAACACGCTGACGGTAAACGGCAAATTGAACGGTC 2902
                   |||      |||   :::|||:::::::||||||:
 848 ...............AsnIleThrThrGlnThrGlyAsnIleAsnGlyL 859

2903 AGGGAACATTCCGCTTTATGTCGGAACTCTTCGGCTACCGCAGCGACAAA 2952
     ::
 859 ys.............................................. 859

2953 TTGAAGCTGGCGGAAAGTTCCGAAGGCACTTACACCTTGGCGGTCAACAA 3002
           :::||||||||||:::|||:::   ||||||   ::::::::
 860 .........ValGluSerSerSerGlySerValThrLeuIleAlaThrGl 873

3003 T............ACCGGCAACGAACCTGCAAGCCTCGAACAATTGACGG 3040
     :            :::||||||      ::::::         :::|||:
 873 yGlnThrLeuAlaValGlyAsnIleSerGlyAspThrValThrIleThrA 890

3041 TAGTGGAAGGAAAAGACAACAAACCGCTGTCCGAAAACCTTAATTTCACC 3090
     ::   :::||||||   :::         |||::::::::::|||   |||
 890 laAspLysGlyLysLeuThrThrGlnThrSerSerLysIleAsnGlyThr 906

seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2000.DAT:AAB01824

seq_documentation_block:
ID   AAB01824 standard; Protein; 1227 AA.
XX
AC   AAB01824;
XX
DT   11-SEP-2000  (first entry)
XX
DE   Haemophilus influenzae strain Joyc HMW1A protein, SEQ ID NO:26.
XX
KW   HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW   non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW   recombinant production; Escherichia coli; antibacterial; vaccine;
KW   human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW   detection; diagnosis.
XX
OS   Haemophilus influenzae strain Joyc.
XX
PN   WO200020609-A2.
XX
PD   13-APR-2000.
XX
PF   07-OCT-1999;   99WO-CA00938.
XX
PR   07-OCT-1998;   98US-0167568.
PR   08-DEC-1998;   98US-0206942.
XX
PA   (CONN-) CONNAUGHT LAB LTD.
XX
PI   Loosmore SM,  Yang Y,  Klein MH;
XX
DR   WPI; 2000-303789/26.
DR   N-PSDB; AAA52175.
XX
PT   Nucleic acid molecule for producing recombinant high molecular weight
PT   proteins of Haemophilus which are used as a vaccine to provide
PT   protection against Haemophilus induced diseases in humans -
XX
PS   Claim 12; Fig 18A-R; 307pp; English.
XX
CC   The invention relates to the recombinant production of Haemophilus
CC   influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC   expression construct used to effect recombinant expression comprises a
CC   promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC   to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC   influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC   clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC   hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC   and the hmwB and hmwC genes encode accessory proteins which are
CC   responsible for post-translational processing and secretion of the HMWA
CC   proteins. The modified hmwABC operon used in the expression construct of
CC   the invention contains an A gene modified such that it encodes only the
CC   mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC   and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC   strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC   vectors are used for the production of recombinant H. influenzae HMW
CC   proteins which can be used as vaccines to mediate a humoral or
CC   cell-mediated immune response to provide protection against diseases in
CC   humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC   pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC   antigens in immunoassays for detecting antibodies against Haemophilus,
CC   HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC   HMW proteins can be used to isolate and clone hmw genes from other
CC   non-typeable strains of Haemophilus via hybridisation reactions. The
CC   present sequence represents an HMWA protein from a non-typeable strain of
CC   H. influenzae.
XX
SQ   Sequence   1227 AA;


alignment_scores:
           Quality:  265.00              Length:    900
             Ratio:  0.559                Gaps:     48
 Percent Similarity:  52.667   Percent Identity: 21.222

alignment_block:
 US-09-303-518D-649 x AAB01824   ..

 Align seg 1/1  to: AAB01824  from: 1  to: 1227

  712 TCAGGTGGTGGCACAGTCAACTTAGGTAGTGAAAAA.....ATTAA 752
      ::::||   ||||||::::::   |||:::   |||        :::::
  152 ThrGlyGlnGlyThrIleThrAlaGlyAsnGlyLysGlyPheArgPheGl 168

  753 ACATAGCCCATATGGTTTTTTACCAACAGGAGGCTCATTTGGC..... 795
      :::::::      :::   :::   ||||||      |||:::
  168 uAsnAlaSerLeuAsnGlyIleGlyThrGlyLeuLeuPheAsnIleLysA 185

  796 ..GACAGTGGCTCACCAATGTTTATCTATGATGCCCAAAAGCAAAAGTGG 843
        |||   |||:::   :::   |||   :::
  185 rgAspLeuGlyAsnAsnPheGlnIleIleAsn.................. 195

  844 TTAATTAATGGGGTATTGCAAACGGGCAACCCCTATATAGGAAAAAGCAA 893
      ::::::||||||:::|||:::   :::            ||||||   ||
  196 PhePheAsnGlyThrLeuAsnIleSer...........GlyLysValAs 208

  894 TGGCTTCCAGCTGGTTCGTAAAGATTGGTTCTATGATGAAATCTTTGCTG 943
      |      :::::::::   |||   |||   |||:::::::   |||   |
  208 nIleSerMetValIleProLysLysTrpAspTyrSerLys...PheArgG 224

  944 GAGATACCCAT......TCAGTATTCTACGAACCACGTCAAAATGGGAAA 987
      ||   |||:::         :::      :::      :::::::::|||
```


224 lyArgThrTyrTrpAsnValThrHisLeuAsnValSerGluGlySerLys 240
988 TACTCTTTTAACGACGATAATAATGGC.....ACAGGAAAAATCAA 1028
241 PheAsnLeuThrIleAspSerArgGlyAspAspThrAlaGlyThrLeuAs 257
1029 TGCCAAACATGAACACAATTCTCTGCCTAATAGATTAAAAACACGAACCG 1078
257 nThrProTyrAsnLeuAsnGlyIleSerPheAsnLysAspThr..... 271
1079 TTCAATTGTTTAATGTT.....TCTTTATCCGAGACAGCAAGA 1116
272 .....IlePheAspValLysGlnAsnGlyAlaValThrPheAspIleLys 286
1117 GAACCTGTTTATCATGCTGCAGGTGGTGTCAACAGTTATCGACCC..... 1161
287 AlaProIle.....GlyValAsnAsnAsnArgAsnLeuAs 298
1162 .....AGACTGAATAATGGAGAAAATATTT 1186
298 nTyrAlaSerPheAsnGlyAsnIleSerValSerGlyGlyGlyAsnValT 315
1187 CCTTT.....ATTGACGAAGGAAAAGGCGAATTG 1215
315 hrPheLysLeuLeuAlaSerSerSerThrAlaGlnThrProGlyValPhe 331
1216 ATACTTACCAGCAACATCAAT...CAAGGTGCTGGAGGATTATATTTCCA 1262
332 IleAsnSerLysHisPheAsnAlaSerGlyGlySerSerLeuGluPheAr 348
1263 AGGAGAT.....TTTACGGTCTCGCCTGAAAATAACG 1294
348 gThrGluGlySerThrLysValGlyPheLeuIleAsn.....AsnAspL 363
1295 AAACTTGGCAAGGCGCGGGCGTTCATATCAGTGAAGACAGTACCGTTACT 1344
363 euThrLeuAsnAlaThrGlyGlyAsnIleSer.....Leu 374
1345 TGGAAAGTAAACGGCGTGGCAAACGACCGCCTGTCCAAAATCGGCAAAGG 1394
375 LeuGlnValGluGlyIleAsp.....GlyMetIleGlyLysGl 387
1395 CACGCTGCACGTTCAAGCCAAAGGGGAAAACCAAGGCTCGATCAGCGTGG 1444
387 y.....ValValAlaLys.....LysAsnIleThrPheA 397
1445 GCGACGGTACAGTCATTTTGGATCAGCAGGCAGACGATAAAGGCAAAAAA 1494
397 laGlyGlyAsnIleThrPhe.....GlySerLys 406
1495 CAAGCCTTTAGTGAAATCGGCTTGGTCAGCGGCAGGGGTACGGTGCAACT 1544
407 LysAlaIleThrGluIle.....GluGlyAsnAlaThrIleAsnAs 420
1545 GAATGCC.....GATAATCAGTTCAACC 1567
420 nAsnAlaAsnValThrLeuIleGlySerAspPheAspAsnHisGlnLysP 437
1568 CC.....GACAAACTCTATTTCGGCTTTCGCGGCGGACGT 1602
437 roLeuThrIleLysLysAspValIle.....IleAsnSerGlyAsn 450
1603 TTGGATTTAAACGGGCATTCGCTTTCGTTCCACCGTATTCAAAATACCGA 1652
451 LeuThrAlaGlyGlyAsnValIleAsnIleAsn..... 461
1653 TGAAGGGGCGATGATTGTCAACCACAATCAAGACAAAGAATCCACCGTTA 1702
462 ....GlyAsnLeuThrValAsnAsnGlyAlaAsnLeuLysAlaIleThrA 477
1703 CCATTACAGGCAATAAAGATATTGCTACAACCGGCAAT.....AACAAC 1746
477 snPheThrPheAsn.....ValGlyGlyLeuPheAspAsn 488
1747 AGCTTGGATAGCAAAAAAGAAATTGCCTACAACGGTTGGTTTGGCGAGAA 1796
489 LysGlyAsnSerAsnIleSerIleAla...ArgGlyGlyAlaLysPheLy 504
1797 AGATACGACCAAAACGAACGGGCGGCTCAACCTTGTTTACCAGCCCGCCG 1846
504 sAspIleAsnAsnThrSerSer...LeuAsnIleThrThrAsnSerAspT 520
1847 CAGAAGACCGCACCCTGCTGCTTTCCGGCGGAACAAATTTAAACGGCAAC 1896
520 hrThrTyrArgThrIleIleGluGlyAsnIleThrAsnLysAlaGlyAsp 536
1897 ATCACGCAAACAAACGGCAAACTGTTTTTCAGCGGCAGACCAACACCGCA 1946
537 LeuAsnIleIleAspAsnLys.....GlyAs 545
1947 CGCCTACAATCATTTAAACGACCATTGGTCGCAAAAAGAGGGCATTCCTC 1996
545 nAlaGluIleGlnIleGlyGlyAsnIleSerGlnLysGlu..... 558
1997 GCGGGGAAATCGTGTGGGACAACGACTGGATCAACCGCACATTTAAAGCG 2046
559 ..GlyAsnLeuThrIleSerSerAspLysIleAsnIleThr..... 571
2047 GAAAACTTCCAAATTAAAGGCGGA..... 2070
572 AsnGlnIleThrIleLysLysGlyValAsnLysGluAspSerAspSerSe 588
2071 .....CAGGCGGTGGTTTCCCGCAATGTTGCCAAAGTGA 2104
588 rThrAlaAsnAsnAlaAsnLeuThrIleLysThrLysGluLeuGlnLeuT 605
2105 AAGGCGATTGGCATTTGAGCAATCACGCCCAAGCAGTTTTTGGTGTCGCA 2154
605 hrGlyAspLeuAsnIleSerGlyPheAspLysAlaGluIle...ThrAla 620
2155 CCGCATCAAAGCCACACAATCTGTACACGTTCGGACTGGACGGGTCTGAC 2204
621 LysGluGlyAlaAspLeuIleIleGlyAsnSerAspAsnAsnAsnAsnAl 637
2205 AAATTGTGTCGAAAAAACC.....ATTACCGACGATAAAGTGATTG 2245
637 aAsnAlaLysLysValThrPheAsnGlnValLysAspSerLysIleSerA 654
2246 CTTCATTGACTAAGACCGACATCAGCGGCAATGTCGATCTTGCC..... 2289
654 laGlySerHisAsnValThrLeuAsnSerLysValGluThrSerAsnGly 670
2290 .....GATCACGCTCATTTAAATCTCAC 2312
671 AsnAsnAspAlaGluSerAsnAsnGlyAspSerThrSerLeuThrIleAs 687
2313 AGGGCTT...GCCACACTCAACGGCAATCTTAGTGCAAATGGCGATACAC 2359
687 nAlaLysAsnValThrValAsnAsnAsnIleThrSerHisLysThrValA 704
2360 GTTATACAGTCAGCCACAACGCCACCCAAAACGGCAACCTTAGCCTC... 2406
704 snIleThrAlaSerGluAsnValThrThrLysAlaGlyThrThrIleAsn 720
2407 .....GTGGGCAATGCCCAAGCAACATTTAATCAAGCCACATTAAACGG 2450
721 AlaThrIleGlySerValGluValThrAlaLysThrGlyAspIleLysGl 737
2451 C.....AACACATCGGCTTCGGGCAATG 2473
737 yGlyIleGluSerAsnSerGlyAsnValAsnIleThrAlaSerGlyAsp. 753
2474 CTTCATTTAATCTAAGCGACCACGCCGTACAAAACGGCAGTCTGACGCTT 2523
754 ..ThrLeuAsnValSerAsnIleThrGlyGlnAsnValThrValAlaAla 769

```
 2524 TCCGGCAACGCTAAGGCAAACGTAAGCCATTCCGCACTCAAC..... 2565
      ::::::::::|||   ::::::::::::   |||::::::|||
  770 AlaSerGlyAlaValThrThrThrLysGlySerThrIleAsnAlaThrTh 786

 2566 .GGTAATGTCTCCCTAGCCGATAAGGCAGTATTCCATTTTGAAAGCAGCC 2614
       ||||||::::::::::::   |||
  786 rGlyAsnAlaAsnIleThrThrLys..................... 794

 2615 GCTTTACCGGACAAATCAGCGGCGGCAAGGATACGGCA.....TTA 2655
           ||||||:::|||::::|||          :::|||       :::
  795 .....ThrGlyGluIleAsnGlyGluValLysSerAlaSerGlyAsnVal 809

 2656 CACTTAAAAGACAGCGAATGGACGCTGCCGTCAGGCACGGAATTAGGCAA 2705
      ::::::      |||      ||||||         ::::::::::::||
  810 AsnIleThrAlaSerGlyAsnThrLeu.....AsnAsnValSerAs 823

 2706 TTTAAACCTTGACAACGCCACCATTACACTCAATTCCGCCTATCGCCACG 2755
      |:::::::   :::|||:::|||:::|||   ||||||:::
  823 nIleThrGlyGlnAsnValThrValThrAlaAsnSerGlyAlaIleThrT 840

 2756 ATGCGGCAGGGGCGCAAACCGGCAGTGCGACA...GATGCGCCGCGCCGC 2802
        :::   |||:::      ::::::::::|||   ||||||
  840 hrThrGluGlySerThrIleAsnAlaThrThrGlyAspAla..... 853

 2803 CGTTCGCGCCGTTCGCGCCGTTCCCTATTATCCGTTACACCGCCAACTTC 2852

  853 ..................................................... 853

 2853 GGTAGAATCCCGTTTCAACACGCTGACGGTAAACGGCAAATTGAACGGTC 2902
                      |||      |||   :::|||:::::::||||||:
  854 ................AsnIleThrThrGlnThrGlyAsnIleAsnGlyL 865

 2903 AGGGAACATTCCGCTTTATGTCGGAACTCTTCGGCTACCGCAGCGACAAA 2952
      ::
  865 ys..................................................... 865

 2953 TTGAAGCTGGCGGAAAGTTCCGAAGGCACTTACACCTTGGCGGTCAACAA 3002
               :::||||||||||:::|||:::   ||||||   ::::::::
  866 .........ValGluSerSerSerGlySerValThrLeuIleAlaThrGl 879

 3003 T............ACCGGCAACGAACCTGCAAGCCTCGAACAATTGACGG 3040
      :           :::||||||      ::::::         :::|||:
  879 yGlnThrLeuAlaValGlyAsnIleSerGlyAspThrValThrIleThrA 896

 3041 TAGTGGAAGGAAAAGACAACAAACCGCTGTCCGAAAACCTTAATTTCACC 3090
      ::   :::||||||   :::         |||:::::::::|||   |||
  896 laAspLysGlyLysLeuThrThrGlnThrSerSerLysIleAsnGlyThr 912

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seq_documentation_block:
ID   AAB01835 standard; Protein; 1095 AA.
XX
AC   AAB01835;
XX
DT   11-SEP-2000  (first entry)
XX
DE   Haemophilus influenzae strain LCDC2 mature HMW1A protein, SEQ ID NO:45.
XX
KW   Mature HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW   non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW   recombinant production; Escherichia coli; antibacterial; vaccine;
KW   human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW   detection; diagnosis.
XX
OS   Haemophilus influenzae strain LCDC2.
XX
PN   WO200020609-A2.
XX
PD   13-APR-2000.
XX
PF   07-OCT-1999;   99WO-CA00938.
XX
PR   07-OCT-1998;   98US-0167568.
PR   08-DEC-1998;   98US-0206942.
XX
PA   (CONN-) CONNAUGHT LAB LTD.
XX
PI   Loosmore SM,  Yang Y,  Klein MH;
XX
DR   WPI; 2000-303789/26.
DR   N-PSDB; AAA52184.
XX
PT   Nucleic acid molecule for producing recombinant high molecular weight
PT   proteins of Haemophilus which are used as a vaccine to provide
PT   protection against Haemophilus induced diseases in humans -
XX
PS   Claim 8; Fig 22A-P; 307pp; English.
XX
CC   The invention relates to the recombinant production of Haemophilus
CC   influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC   expression construct used to effect recombinant expression comprises a
CC   promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC   to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC   influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC   clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC   hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC   and the hmwB and hmwC genes encode accessory proteins which are
CC   responsible for post-translational processing and secretion of the HMWA
CC   proteins. The modified hmwABC operon used in the expression construct of
CC   the invention contains an A gene modified such that it encodes only the
CC   mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC   and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC   strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC   vectors are used for the production of recombinant H. influenzae HMW
CC   proteins which can be used as vaccines to mediate a humoral or
CC   cell-mediated immune response to provide protection against diseases in
CC   humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC   pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC   antigens in immunoassays for detecting antibodies against Haemophilus,
CC   HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC   HMW proteins can be used to isolate and clone hmw genes from other
CC   non-typeable strains of Haemophilus via hybridisation reactions. The
CC   present sequence represents a mature HMWA protein from a non-typeable
CC   strain of H. influenzae.
XX
SQ   Sequence   1095 AA;


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              Ratio:  0.442                Gaps:     56
 Percent Similarity:  51.865   Percent Identity: 20.035

alignment_block:
 US-09-303-518D-649 x AAB01835   ..

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    1 ProAspGluValThrIleGlyAlaGly...AspValGlyArgSerAspAs 16

  624 AGAT..........................GAGCCCAATAACCGCG 643
      :::: '                       |||   |||:::   :
   16 pSerSerAspThrAlaPheProThrGlyThrGlyGluArgAsnSerProL 33

  644 AAAGTTCATATCATATTGCAAGTGCGTATTCTTGGCTCGTTGGTGGCAAT 693
      ::::::::   :::         :::   :::               |||
   33 ysThrAsnAlaGlnAsnArgProThrIleThr..............Asn 44

  694 ACCTTTGCACAAAATGGATCAGGTGGTGGCACA...GTCAACTTAGGTAG 740
      |||      ::::::         :::||||||   ||||||:::   ::
   45 ThrSerLeuGluGlnIleLeuLysAsnGlyThrPheValAsnIleThrAl 61

  741 TGAA........................AAAATTAAACATAGCCCAT 763
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2219 AAACC.........ATTACCGACGATAAAGTGATTGCTTCATTGACTAAG 2259
637 alThrPheAsnGlnValLysAspSerLysIleSerAlaAspSerHisAsn 653

2260 ACCGACATCAGCGGCAATGTCGATCTTGCC.....................  2289
654 ValThrLeuAsnSerLysValGluThrSerAsnGlyAsnAsnAspAlaGl 670

2290 .............GATCACGCTCATTTAAATCTCACAGGGCTT...GCCA 2323
670 uSerAsnAsnGlyAspGlyThrSerLeuThrIleAsnAlaLysAsnIleT 687

2324 CACTCAACGGCAATCTTAGTGCAAATGGCGATACACGTTATACAGTCAGC 2373
687 hrValAsnAsnAsnIleThrSerHisLysThrValAsnIleThrAlaSer 703

2374 CACAACGCCACCCAAAACGGCAACCTTAGCCTC.........GTGGGCAA 2414
704 GluAsnValThrThrLysAlaGlyThrThrIleAsnAlaThrThrGlySe 720

2415 TGCCCAAGCAACATTTAATCAAGCCACATTAAACGGCAACACA...TCGG 2461
720 rValGluValThrAlaLysThrGlyAspIleLysGlyLysValGluSerT 737

2462 CTTCGGGCAATGCTTCATTTAATCTAAGCGACCACGCC..... 2499
737 hrSerGlySerValThrLeuThrAlaThrGlyGluAlaLeuAlaValSer 753

2500 ...GTACAAAACGGCAGTCTGACGCTTTCCGGCAAC..... 2532
754 AsnIleSerGlyAsnThrValThrIleThrAlaAsnLysGlyLysLeuTh 770

2533 .GCTAAGGCAAACGTAAGCCATTCCGCACTCAACGGTAATGTCTCCCTAG 2581
770 rThrGlnAlaGlySerThrValSerAlaIleAsnGlyValThrAlaSerS 787

2582 CCGATAAGGCAGTATTCCATTTTGAAAGCAGCCGCTTTACCGGACAAATC 2631
787 er.....GlnSerGlyAspIleSerGlyThrIle 796

2632 AGCGGCGGC......AAGGATACGGCATTACACTTAAAAGACAGCGAATG 2675
797 SerGlyAsnThrValLysValSerAlaIle.....GlyAspLe 809

2676 GACGCTGCCGTCAGGCACGGAATTA.....GGCAATTTAAACC 2713
809 uThrThrLysSerGlySerGluIleLysAlaLysThrGlyGluAlaAsnV 826

2714 TTGACAACGCCACCATTACACTCAATTCCGCCTATCGCCACGATGCGGCA 2763
826 alThrSerAlaThrGlyThrIleGlyGlyThrIleSerGlyAsnAlaVal 842

2764 GGG......GCGCAAACCGGCAGTGCGACA......GATGCGCCGCGCCG 2801
843 AsnValThrAlaAsnThrGlyAspLeuThrValGluAspAlaAlaLysIl 859

2802 CCGTTCGCGCCGTTCGCGCCGTTCCCTATTATCCGTTACACCGCCAACTT 2851
859 eAspAlaThrGlyGlyAlaAlaThrLeuThrAlaThrSerGlyLysLeuT 876

2852 CGGTAGAATCCCGTTTCAACACGCTGACGGTAAACGGCAAATTGAACGGT 2901
876 hrThrLysAlaSerSerSerIleThrSerAlaAsnAsnGlnValAsn... 891

2902 CAGGGAACATTCCGCTTTATGTCGGAACTCTTCGGCTACCGCAGCGACAA 2951

891 ..................................................  891

2952 ATTGAAGCTGGCGGAAAGTTCCGAAGGCACTTACACCTTGGCGGTCAACA 3001
892 .LeuSerAlaLysAspGlySerIleGlyGlyAsnIleAsnAlaAlaAsnV 908

3002 ATACCGGCAACGAACCTGCAAGCCTCGAACAATTG..... 3036
908 alThrLeuAsnThrThrGlyAlaLeuThrThrValLysGlySerSerIle 924

3037 .................ACGGTAGTGGAAGGAAAAGAC.....AA 3059
925 AsnAlaAsnSerGlyThrLeuValIleAsnAlaLysAspAlaGluLeuAs 941

3060 CAAACCGCTGTCCGAAAAC.....CTTAATTTCACCCTGCAAAACG 3100
941 nGlyGluAlaSerGlyAsnHisThrValValAsnAlaThrAsnAlaAsnG 958

3101 AACACGTCGATGCCGGCGCGTGGCGTTACCAACTCATCCGCAAAGACGGC 3150
958 lySerGlySerValIleAlaThrThrSerSerArgValAsnIleThrGly 974

3151 GAGTTCCGCCTGCATAATCCGGTCAAAGAACAAGAGCTTTCCGACAAACT 3200
975 AspLeuIleThrIleAsnGlyLeu.....AsnIleIleSerLysAs 988

3201 CGGCAAGGCAGAAGCCAAAAAACAGGCGGAAAAAGACAACGCGCAA.... 3246
988 nGlyIleAsnThrValLeuLeuLysGlyValLysIleAspValLysTyrI 1005

3247 .................AGCCTTGACGCGCTGATTGCGGCCGGGCGCGAT 3279
1005 leGlnProGlyIleAlaSerValAspGluValIleGluAlaLysArg... 1020

3280 GCCGTCGAAAAGACAGAAAGCGTTGCCGAACCGGCCCGGCAGGCAGGCGG 3329
1021 IleLeuGluLysValLysAspLeuSerAspGluGluArgGluAlaLeuAl 1037

3330 GGAA...AATGTCGGCATTATGCAGGCGGAGGAAGAGAAAAAACGGGTGC 3376
1037 aLysLeuGlyValSerAlaValArgPheAlaGluProAsnAsnAlaIle. 1053

3377 AGGCGGATAAAGACACCGCCTTGGCGAAACAGCGCGAAGCGGAAACCCGG 3426
1054 .................ThrIleAsnThrGlnAsnGluPheThrThrArg 1064

3427 CCGGCTACC 3435
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seq_documentation_block:

ID AAB01834 standard; Protein; 1101 AA.
XX
AC AAB01834;
XX
DT 11-SEP-2000 (first entry)
XX
DE Haemophilus influenzae strain LCDC2 HMW1A protein, SEQ ID NO:43.
XX
KW HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW recombinant production; Escherichia coli; antibacterial; vaccine;
KW human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW detection; diagnosis.
XX
OS Haemophilus influenzae strain LCDC2.
XX
PN WO200020609-A2.
XX
PD 13-APR-2000.
XX
PF 07-OCT-1999; 99WO-CA00938.
XX
PR 07-OCT-1998; 98US-0167568.
PR 08-DEC-1998; 98US-0206942.
XX
PA (CONN-) CONNAUGHT LAB LTD.

XX
PI Loosmore SM, Yang Y, Klein MH;
XX
DR WPI; 2000-303789/26.
DR N-PSDB; AAA52183.
XX
PT Nucleic acid molecule for producing recombinant high molecular weight
PT proteins of Haemophilus which are used as a vaccine to provide
PT protection against Haemophilus induced diseases in humans -
XX
PS Claim 12; Fig 22A-P; 307pp; English.
XX
CC The invention relates to the recombinant production of Haemophilus
CC influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC expression construct used to effect recombinant expression comprises a
CC promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC and the hmwB and hmwC genes encode accessory proteins which are
CC responsible for post-translational processing and secretion of the HMWA
CC proteins. The modified hmwABC operon used in the expression construct of
CC the invention contains an A gene modified such that it encodes only the
CC mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC vectors are used for the production of recombinant H. influenzae HMW
CC proteins which can be used as vaccines to mediate a humoral or
CC cell-mediated immune response to provide protection against diseases in
CC humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC antigens in immunoassays for detecting antibodies against Haemophilus,
CC HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC HMW proteins can be used to isolate and clone hmw genes from other
CC non-typeable strains of Haemophilus via hybridisation reactions. The
CC present sequence represents an HMWA protein from a non-typeable strain of
CC H. influenzae.
XX
SQ Sequence 1101 AA;

alignment_scores:
Quality: 264.50 Length: 1153
Ratio: 0.442 Gaps: 56
Percent Similarity: 51.865 Percent Identity: 20.035

alignment_block:
US-09-303-518D-649 x AAB01834 ..

Align seg 1/1 to: AAB01834 from: 1 to: 1101

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574 CCTGACCGTGTTCGTATTGGGGCAGGCAGGCAATATTGGCGATCTGATGA 623
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  7 ProAspGluValThrIleGlyAlaGly...AspValGlyArgSerAspAs 22

624 AGAT..........................GAGCCCAATAACCGCG 643
    ::::                          |||  |||:::  :
 22 pSerSerAspThrAlaPheProThrGlyThrGlyGluArgAsnSerProL 39

644 AAAGTTCATATCATATTGCAAGTGCGTATTCTTGGCTCGTTGGTGGCAAT 693
    ::::::::  :::        :::  :::               |||
 39 ysThrAsnAlaGlnAsnArgProThrIleThr.............Asn 50

694 ACCTTTGCACAAAATGGATCAGGTGGTGGCACA...GTCAACTTAGGTAG 740
    |||     ::::::       :::||||||  ||||||:::  ::
 51 ThrSerLeuGluGlnIleLeuLysAsnGlyThrPheValAsnIleThrAl 67

741 TGAA........................AAAATTAAACATAGCCCAT 763
    ::::                       :::||||||:::::  :
 67 aLysAsnLysIleLeuValAsnSerAspIleAsnIleLysGluAsnSerH 84

764 AT..............................GGTTTTTTACCAACA 780
    ::                                |||
 84 isLeuIleLeuTrpSerGluArgAspGlyAsnSerGlyValGlnIleAsp 100

781 GGAGGCTCATTTGGCGACAGTGGCTCACCAATGTTTATCTAT........ 822
    |||:::     :::   :::|||:::  :::   :::|||
101 GlyAsnIleThrSerAlaThrGlyGlySerLeuThrValTyrSerSerGl 117

823 .......GATGCCCAAAAGCAAAAGTGGTTAATTAATGGGGTATTG.... 861
        |||:::::::|||:::     |||   :::|||   |||
117 yTrpValAspValHisLysAsnIleThrLeuAsnSerGlyTyrLeuAsnI 134

862 ........CAAACGGGCAACCCCTATATAGGAAAAAGCAATGGCTTCCAG 903
         ::::::|||:::     :::   :::::::|||   :::
134 leThrThrLysSerGlyAspValAlaPheGluGlnGlyAsnAspLeuThr 150

904 CTGGTT.......................CGTAAAGATTGGTTCTATGA 929
    ::::::                       :::|||  :::   :::||
151 IleThrGlyGlnGlyThrIleThrAlaSerLysLysGlyPheArgPheAs 167

930 TGAAATCTTTGCTGGAGATACCCATTCAGTATTC.........TACGAAC 970
    |::::::     :::  :::   :::   |||         |||:::
167 pAsnValThrLeuSerGlyValLysLysGlyPheLeuPheLysTyrSerG 184

971 CACGTCAAAATGGGAAATACTCT..............TTTAACGACGAT 1005
       :::|||:::|||   |||               |||:::
184 lnThrAsnAsnAsnLysAspSerAsnPheGluAsnHisPheArgGlyThr 200

1006 AATAATGGCACAGGAAAAATC............................ 1026
     |||   :::||||||:::
201 LeuAsnIleSerGlyLysValAspIleLeuMetGlnAlaArgGlnGluAs 217

1027 ....AATGCCAAACATGAACACAATTCTCTGCCTAAT......AGATTAA 1066
        |||   :::|||:::   :::|||      |||      ||||||:
217 nTrpAsnArgArgHisSerGlyArgSerHisTrpAsnValThrArgLeuA 234

1067 AAACACGAACCGTTCAATTGTTTAATGTTTCTTTATCCGAGACAGCAAGA 1116
     :::::   |||   :::   :::|||:::::::::::::::::::::::
234 snValSerThrAsnSerTyrLeuAsnIleThrIleAspAsnSerGlySer 250

1117 GAACCTGTTTATCATGCTGCAGGTGGTGTCAACAGTTATCGACCCAGACT 1166
     :::|||         :::   |||:::         ||||||
251 ArgPro.........SerProGlyAlaGlyProLeuTyrArgArgSerGl 264

1167 GAATAATGGA.........GAAAATATTTCCTTTATTGACGAAGGAAAAG 1207
        ||||||         :::|||  :::   ::::::   ::::::|
264 yLeuAsnGlyIleSerPheAsnAsnAspThrValPheAsnValAlaSerG 281

1208 GCGAATTGATA.....................CTTACCAGCAACATCAAT 1236
     ||:::   :::                    ::::::||||||::::::
281 lySerAlaValAsnPheSerIleLysProProIleValSerAsnValHis 297

1237 CAAGGTGCTGGAGGATTATATTTCCAAGGAGATTTTACGGTCTCGCCTGA 1286
     :::|||         |||   |||:::|||:::   :::|||
298 AspGlyAsnHisThrLeu...PheAsnGlyAsnValSerVal........ 310

1287 AAATAACGAAACTTGGCAAGGCGCGGGC.........GTTCATATCAGTG 1327
                        |||:::|||            |||::::::
311 ................LeuGlyGlyGlyAspValAsnPheHisPheAsnA 322

1328 AAGACAGTACCGTTACTTGGAAAGTAAACGGCGTGGCAAACGACCGCCTG 1377
       :::|||:::      |||      :::   |||   :::::::::
322 laSerSerSerAsnHisTrpThrHisGlyValValIleLysSerGlnAsn 338

1378 TCCAAAATCGGCAAAGGC...ACGCTGCACGTTCAAGCCAAAGGG..... 1419
        :::   :::::::|||   :::|||:::   :::::::::|||
339 PheAsnAlaSerGluGlySerSerLeuArgPheLysSerGluGlySerTh 355

1420 ..................GAAAACCAAGGCTCGATCAGCGTGGGCGACG 1450
                        |||::::::   ::::::::::::      |
355 rArgThrAlaPheThrIleGluSerAspLeuThrLeuAsnAlaThrGlyG 372

1451 GTACAGTCATTTTGGATCAGCAGGCAGACGATAAAGGCAAAAAACAAGCC 1500
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```

```
 372 lyAsnIleSerLeuAsnGlnValAlaGlyIleAspGlyAsnLeuGlnLys 388

1501 TTTAGTGAAATCGGCTTGGTCAGCGGCAGG.................GG 1532
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 389 ............SerLeuValAlaAsnLysAsnIleThrPheGluGlyGl 401

1533 TACGGTGCAACTGAATGCCGATAATCAGTTCAACCCCGACAAACTCTATT 1582
     |:::::   |||   |||                  ||||||      :
 401 yAsnIleThrLeuAlaAla.................AspLysLysProI 412

1583 TCGGCTTTCGCGGCGGACGTTTGGATTTAAACGGGCATTCGCTTTCGTTC 1632
     ::   ::::::|||:::            :::|||   ::::::::::::
 412 leGluIleLysGlyAsnIleThrValLysGluGlyAlaAsnValThrLeu 428

1633 CACCGTATTCAA...AATACCGATGAAGGGGCGATGATTGTCAACCACAA 1679
     :::      :::   ::::::|||:::::::|||:::   ::::::   ||
 429 ArgSerAlaAsnTyrGlyAsnAspLysSerAlaLeuSerIleArgGlyAs 445

1680 TCAAGACAAAGAATCCACCGTTACCATTACAGGCAAT.............. 1716
     |      ::::::::::::::::|||:::||||||:::
 445 nValThrAsnLysGlyAsnLeuThrValThrGlySerAlaIleAsnIleG 462

1717 ..AAAGATATTGCTACAACCGGCAAT......................... 1740
       |||:::::::::::::   |||:::
 462 luLysAsnLeuThrValGluGlySerAlaLysPheLeuAlaAsnProAsn 478

1741 ..........................AACAACAGCTTGGATAGCAAAAA 1763
                              :::|||:::      |||:::
 479 TyrSerPheAsnValSerGlyLeuPheAspAsnGlnGlyLysSerAsnIl 495

1764 AGAAATTGCCTACAACGGT...TGGTTTGGCGAGAAAGATACGACCAAAA 1810
      :::|||||||   :::|||      |||   :::   :::::||||||:
 495 eSerIleAlaLysGlyGlyAlaHisPheLysAspIleAsnAsnThrLysS 512

1811 CGAACGGGCGGCTCAACCTTGTTTACCAGCCCGCCGCAGAAGACCGCACC 1860
     ::         ||||||::::::   :::      :::      ||||||
 512 er.........LeuAsnIleThrThrAsnSerAspSerAlaTyrArgThr 525

1861 CTGCTGCTTTCCGGCGGAACAAATTTAAACGGCAACATCACGCAAACAAA 1910
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 526 IleIleGluGlyAsnIleThrAsnSerAsnGlyAspLeuAsnIleThrAs 542

1911 CGGCAAACTGTTTTTCAGCGGCAGACCAACACCGCACGCCTACAATCATT 1960
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 542 pAsnLys.......................AsnAsnAlaGluIleGlnI 551

1961 TAAACGACCATTGGTCGCAAAAAGAGGGCATTCCTCGCGGGGAAATCGTG 2010
     :::::   :::   ||||||||||||            |||:::::::::
 551 leGlyGlyAsnIleSerGlnLysGlu............GlyAsnLeuThr 563

2011 TGGGACAACGACTGGATCAACCGCACATTTAAAGCGGAAAACTTCCAAAT 2060
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 564 IleSerSerAspLysIleAsnIleThr.........AsnGlnIleThrIl 577

2061 TAAAGGCGGA..................................... 2070
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 577 eLysLysGlyValAsnLysGluAspSerAspSerSerThrAlaAsnAsnA 594

2071 ..CAGGCGGTGGTTTCCCGCAATGTTGCCAAAGTGAAAGGCGATTGGCAT 2118
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 594 laAsnLeuThrIleLysThrLysGluLeuGlnLeuThrGlyAspLeuAsn 610

2119 TTGAGCAATCACGCCCAAGCAGTTTTTGGTGTCGCACCGCATCAAAGCCA 2168
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 611 IleSerGlyPheAspLysAlaGluIle...ThrAlaLysGluGlyAlaAs 626

2169 CACAATCTGTACACGTTCGGACTGGACGGGTCTGACAAATTGTGTCGAAA 2218
        |||      :::||||||   ::::::   :::|||:::   :::
 626 pLeuIleIleGlyAsnSerAspAsnAsnAsnAsnAlaAsnAlaLysLysV 643

2219 AAACC.........ATTACCGACGATAAAGTGATTGCTTCATTGACTAAG 2259
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 643 alThrPheAsnGlnValLysAspSerLysIleSerAlaAspSerHisAsn 659

2260 ACCGACATCAGCGGCAATGTCGATCTTGCC..................... 2289
     :::   ::::::::::::|||:::   :::
 660 ValThrLeuAsnSerLysValGluThrSerAsnGlyAsnAsnAspAlaGl 676

2290 .............GATCACGCTCATTTAAATCTCACAGGGCTT...GCCA 2323
                  |||   :::   |||:::::::::::::         |
 676 uSerAsnAsnGlyAspGlyThrSerLeuThrIleAsnAlaLysAsnIleT 693

2324 CACTCAACGGCAATCTTAGTGCAAATGGCGATACACGTTATACAGTCAGC 2373
     ||:::|||:::|||::::::::::::      ::::::   |||:::|||
 693 hrValAsnAsnAsnIleThrSerHisLysThrValAsnIleThrAlaSer 709

2374 CACAACGCCACCCAAAACGGCAACCTTAGCCTC.........GTGGGCAA 2414
     :::|||:::|||   :::::::::   ::::::          :::|||::
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2415 TGCCCAAGCAACATTTAATCAAGCCACATTAAACGGCAACACA...TCGG 2461
     ::::::::::|||   :::   :::   ::::::|||::::::   |||:
 726 rValGluValThrAlaLysThrGlyAspIleLysGlyLysValGluSerT 743

2462 CTTCGGGCAATGCTTCATTTAATCTAAGCGACCACGCC............. 2499
     ::||||||:::::::::::::::   :::   :::|||
 743 hrSerGlySerValThrLeuThrAlaThrGlyGluAlaLeuAlaValSer 759

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 760 AsnIleSerGlyAsnThrValThrIleThrAlaAsnLysGlyLysLeuTh 776

2533 .GCTAAGGCAAACGTAAGCCATTCCGCACTCAACGGTAATGTCTCCCTAG 2581
      ::::::|||:::   :::   ||||||:::||||||   ::::::   :
 776 rThrGlnAlaGlySerThrValSerAlaIleAsnGlyValThrAlaSerS 793

2582 CCGATAAGGCAGTATTCCATTTTGAAAGCAGCCGCTTTACCGGACAAATC 2631
     ::                    :::|||:::   :::::|||   |||
 793 er.....................GlnSerGlyAspIleSerGlyThrIle 802

2632 AGCGGCGGC......AAGGATACGGCATTACACTTAAAAGACAGCGAATG 2675
     |||||||:::      |||   :::|||:::             ::::::
 803 SerGlyAsnThrValLysValSerAlaIle............GlyAspLe 815

2676 GACGCTGCCGTCAGGCACGGAATTA............GGCAATTTAAACC 2713
      |||      ||||||:::|||:::            |||:::   |||:
 815 uThrThrLysSerGlySerGluIleLysAlaLysThrGlyGluAlaAsnV 832

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 849 AsnValThrAlaAsnThrGlyAspLeuThrValGluAspAlaAlaLysIl 865

2802 CCGTTCGCGCCGTTCGCGCCGTTCCCTATTATCCGTTACACCGCCAACTT 2851
        :::      :::      :::|||  :::::::::          :
 865 eAspAlaThrGlyGlyAlaAlaThrLeuThrAlaThrSerGlyLysLeuT 882

2852 CGGTAGAATCCCGTTTCAACACGCTGACGGTAAACGGCAAATTGAACGGT 2901
     ::::::::::      :::      ::::::|||::::::::|||
 882 hrThrLysAlaSerSerSerIleThrSerAlaAsnAsnGlnValAsn... 897

2902 CAGGGAACATTCCGCTTTATGTCGGAACTCTTCGGCTACCGCAGCGACAA 2951

 897 ................................................. 897

2952 ATTGAAGCTGGCGGAAAGTTCCGAAGGCACTTACACCTTGGCGGTCAACA 3001
      |||:::      ::::::|||   |||            |||:::|||
 898 .LeuSerAlaLysAspGlySerIleGlyGlyAsnIleAsnAlaAlaAsnV 914

3002 ATACCGGCAACGAACCTGCAAGCCTCGAACAATTG............... 3036
       |||   |||      ::::::|||      :::
 914 alThrLeuAsnThrThrGlyAlaLeuThrThrValLysGlySerSerIle 930
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    3037 ..................ACGGTAGTGGAAGGAAAAGAC.........AA 3059
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     931 AsnAlaAsnSerGlyThrLeuValIleAsnAlaLysAspAlaGluLeuAs 947

    3060 CAAACCGCTGTCCGAAAAC.........CTTAATTTCACCCTGCAAAACG 3100
         |         |||   |||          :::|||   |||      |||
     947 nGlyGluAlaSerGlyAsnHisThrValValAsnAlaThrAsnAlaAsnG 964

    3101 AACACGTCGATGCCGGCGCGTGGCGTTACCAACTCATCCGCAAAGACGGC 3150
              ::::::   |||        :::   ::::::      |||
     964 lySerGlySerValIleAlaThrThrSerSerArgValAsnIleThrGly 980

    3151 GAGTTCCGCCTGCATAATCCGGTCAAAGAACAAGAGCTTTCCGACAAACT 3200
         ::::::         |||   :::         ::::::   :::|||
     981 AspLeuIleThrIleAsnGlyLeu.........AsnIleIleSerLysAs 994

    3201 CGGCAAGGCAGAAGCCAAAAAACAGGCGGAAAAAGACAACGCGCAA.... 3246
          |||         :::      ::::::   |||   :::::::::
     994 nGlyIleAsnThrValLeuLeuLysGlyValLysIleAspValLysTyrI 1011

    3247 ..................AGCCTTGACGCGCTGATTGCGGCCGGGCGCGAT 3279
                            |||:::|||   :::|||   |||   |||
    1011 leGlnProGlyIleAlaSerValAspGluValIleGluAlaLysArg... 1026

    3280 GCCGTCGAAAAGACAGAAAGCGTTGCCGAACCGGCCCGGCAGGCAGGCGG 3329
            :::|||||||:::::::::::::::::::      |||:::|||   ::
    1027 IleLeuGluLysValLysAspLeuSerAspGluGluArgGluAlaLeuAl 1043

    3330 GGAA...AATGTCGGCATTATGCAGGCGGAGGAAGAGAAAAAACGGGTGC 3376
         ::::   :::|||:::   ::::::      |||   ::::::   :::
    1043 aLysLeuGlyValSerAlaValArgPheAlaGluProAsnAsnAlaIle. 1059

    3377 AGGCGGATAAAGACACCGCCTTGGCGAAACAGCGCGAAGCGGAAACCCGG 3426
                        ::::::      |||:::|||      ||||||
    1060 .................ThrIleAsnThrGlnAsnGluPheThrThrArg 1070

    3427 CCGGCTACC 3435
         |||::::::
    1071 ProSerSer 1073
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seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2001.DAT:AAU34143

seq_documentation_block:

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ID   AAU34143 standard; Protein; 2086 AA.
XX
AC   AAU34143;
XX
DT   14-FEB-2002  (first entry)
XX
DE   Staphylococcus aureus cellular proliferation protein #419.
XX
KW   Antisense; prokaryotic cellular proliferation protein;
KW   antibiotic; antibacterial; drug design.
XX
OS   Staphylococcus aureus.
XX
PN   WO200170955-A2.
XX
PD   27-SEP-2001.
XX
PF   21-MAR-2001; 2001WO-US09180.
XX
PR   21-MAR-2000; 2000US-191078P.
PR   23-MAY-2000; 2000US-206848P.
PR   26-MAY-2000; 2000US-207727P.
PR   23-OCT-2000; 2000US-242578P.
PR   27-NOV-2000; 2000US-253625P.
PR   22-DEC-2000; 2000US-257931P.
PR   16-FEB-2001; 2001US-269308P.
XX
PA   (ELIT-) ELITRA PHARM INC.
XX
PI   Haselbeck R,  Ohlsen KL,  Zyskind JW,  Wall D,  Trawick JD,  Carr GJ;
PI   Yamamoto RT,  Xu HH;
XX
DR   WPI; 2001-611495/70.
DR   N-PSDB; AAS52002.
XX
PT   New polynucleotides for the identification and development of
PT   antibiotics, comprise sequences of antisense nucleic acids -
XX
PS   Example 3; Seq ID No 5639; 511pp; English.
XX
CC   The invention relates to antisense inhibitors of genes essential to
CC   prokaryotic cellular proliferation, their use in identifying the
CC   genes, their use in the discovery of novel antibiotics, the essential
CC   genes themselves and the encoded proteins. The prokaryotes used are
CC   Escherichia coli, Staphylococcus aureus, Salmonella typhi, Klebsiella
CC   pneumoniae, Pseudomonas aeruginosa and Enterococcus faecalis. The
CC   invention is also useful for the identification of potential new targets
CC   for antibiotic development. The antisense nucleic acids can also be used
CC   to identify proteins used in proliferation, to express these proteins,
CC   and to obtain antibodies capable of binding to the expressed proteins.
CC   The proteins can be used to screen compounds in rational drug discovery
CC   programmes. The antisense nucleic acid sequence is also useful to screen
CC   for homologous nucleic acids which are required for cell proliferation in
CC   a wide variety of organisms. The present sequence represents an
CC   essential prokaryotic cellular proliferation protein.
CC   Note: The sequence data for this patent did not form part
CC   of the printed specification, but was obtained in electronic
CC   format directly from WIPO at
CC   ftp.wipo.int/pub/published_pct_sequences.
XX
SQ   Sequence   2086 AA;
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alignment_scores:

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           Quality:  264.50            Length:   1388
             Ratio:  0.387               Gaps:     69
 Percent Similarity:  49.207   Percent Identity: 20.605
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alignment_block:

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 US-09-303-518D-649 x AAU34143   ..

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     543 TGGGCGGAAATATATCGATCAAAATAATTACCCTGACCGTGTTCGTATTG 592
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     713 nAlaLysGlyIleIleAsnGlnThrAsnAsnPro................. 724

     593 GGGCAGGCAGGCAATATTGGCGATCTGATGAAGATGAGCCCAATAACCGC 642

     724 ................................................. 724

     643 GAAAGTTCATATCATATTGCAAGTGCGTATTCTTGGCTCGTTGGTGGCAA 692
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     725 ..................ThrMetAspThrSerAlaIleThrGlnAlaTh 735

     693 TACCTTTGCACAAAATGGATCAGGTGGTGGCACAGTCAACTTAGGTAGTG 742
         :|||   ::::::|||:::::::::|||      :::|||   |||:::|
     735 rThrGlnValAsnAsnAlaLysAsnGly......LeuAsn...GlyAlaG 749

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     749 luAsnLeuArgAsn.AlaGlnAsnThrAlaLysGln.........AsnLe 762

     793 GGCGACAGTGGCTCACCAATGTTTATCTATGATGCCCAAAAGCAAAAGTG 842
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     762 uAsnThrLeuSerHis..............LeuThrAsnAsnGlnLysS 774

     843 GTTAATTAATGGGGTATTGCAAACGGGCAACCCCTATATAGGAAAAAGCA 892
         ::   :::   :::         ||||||      :::   |||   :::
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774 erAlaIleSerSerGlnIleAspArgAlaGlyHisValSerGluValThr 790
893 ATGGCTTCCAGCTGGTTCGTAAAGATTGGTTCTATGATGAAATCTTTGCT 942
791 AlaAlaLysAsnAlaAlaThrGluLeuAsnThrGlnMetGlyAsnLeuGl 807
943 GGAGATACCCATTCAGTATTCTACGAACCACGTCAAAATGGGAAATACTC 992
807 uGln.....AlaIleHisAspGlnAsnThrValLysGlnGly..ValAs 821
993 TTTTAACGACGATAATAATGGCACAGGAAAAATCAATGCCAAACATGAAC 1042
821 nPheThrAspAlaAsp.....LysAlaLysA 830
1043 ACAATTCTCTGCCTAATAGATTAAAAACACGAACCGTTCAATTGTTTAAT 1092
830 rgAspAlaTyrThrAsnAlaValSerArgAlaGluThrIleLeuAsnLys 846
1093 GTTTCTTTATCCGAGACAGCAAGAGAACCTGTTTATCATGCTGCAGGTGG 1142
847 ThrGlnGlyAlaAsnThrSerLysGlnAspValGluAlaAlaIleGlnAs 863
1143 TGTCAACAGTTATCGACCCAGACTGAATAATGGAGAAAATATTTCCTTTA 1192
863 nValThrSerAlaLysAsnAlaLeuAsnGlyAspGlnAsnValThrAsnA 880
1193 TT...GACGAAGGAAAAGGCGAATTGATACTTACCAGCAACATCAATCAA 1239
880 laLysAsnThrAlaLysHisAlaLeuAsnAsnLeuThrSerIleAsnAsn 896
1240 GGTGCTGGAGGATTATATTTCCAAGGAGATTTTACGGTCTCGCCTGAAAA 1289
897 AlaGln.....LysArgAspLeuThrThrLysIleAspGl 908
1290 TAACGAAACTTGGCAAGGCGCGGGCGTTCATATCAGTGAAGACAGTACCG 1339
908 nAlaThrThrValAlaGly..... 914
1340 TTACTTGGAAAGTAAACGGCGTGGCAAACGACCGCCTGTCCAAAATCGGC 1389
915 .....ValGluAlaValSerAsn..... 920
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seq_documentation_block:
ID   AAU37017 standard; Protein; 5795 AA.
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AC   AAU37017;
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DT   14-FEB-2002  (first entry)
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DE   Staphylococcus aureus cellular proliferation protein #1187.
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KW   Antisense; prokaryotic cellular proliferation protein;
KW   antibiotic; antibacterial; drug design.
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OS   Staphylococcus aureus.
XX
PN   WO200170955-A2.
XX
PD   27-SEP-2001.
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PF   21-MAR-2001; 2001WO-US09180.
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PR   21-MAR-2000; 2000US-191078P.
PR   23-MAY-2000; 2000US-206848P.
PR   26-MAY-2000; 2000US-207727P.
PR   23-OCT-2000; 2000US-242578P.
PR   27-NOV-2000; 2000US-253625P.
PR   22-DEC-2000; 2000US-257931P.
PR   16-FEB-2001; 2001US-269308P.
XX
PA   (ELIT-) ELITRA PHARM INC.
XX
PI   Haselbeck R,  Ohlsen KL,  Zyskind JW,  Wall D,  Trawick JD,  Carr GJ;
PI   Yamamoto RT,  Xu HH;
XX
DR   WPI; 2001-611495/70.
DR   N-PSDB; AAS54876.
XX
PT   New polynucleotides for the identification and development of
PT   antibiotics, comprise sequences of antisense nucleic acids -
XX
PS   Example 3; Seq ID No 12610; 511pp; English.
XX
CC   The invention relates to antisense inhibitors of genes essential to
CC   prokaryotic cellular proliferation, their use in identifying the
CC   genes, their use in the discovery of novel antibiotics, the essential
CC   genes themselves and the encoded proteins. The prokaryotes used are
CC   Escherichia coli, Staphylococcus aureus, Salmonella typhi, Klebsiella
CC   pneumoniae, Pseudomonas aeruginosa and Enterococcus faecalis. The
CC   invention is also useful for the identification of potential new targets
CC   for antibiotic development. The antisense nucleic acids can also be used
CC   to identify proteins used in proliferation, to express these proteins,
CC   and to obtain antibodies capable of binding to the expressed proteins.
CC   The proteins can be used to screen compounds in rational drug discovery
CC   programmes. The antisense nucleic acid sequence is also useful to screen
CC   for homologous nucleic acids which are required for cell proliferation in
CC   a wide variety of organisms. The present sequence represents an
CC   essential prokaryotic cellular proliferation protein.
CC   Note: The sequence data for this patent did not form part
CC   of the printed specification, but was obtained in electronic
CC   format directly from WIPO at
CC   ftp.wipo.int/pub/published_pct_sequences.
XX
SQ   Sequence   5795 AA;


alignment_scores:
           Quality:  264.50              Length:   1388
             Ratio:  0.387                 Gaps:     69
 Percent Similarity:  49.207   Percent Identity: 20.605

alignment_block:
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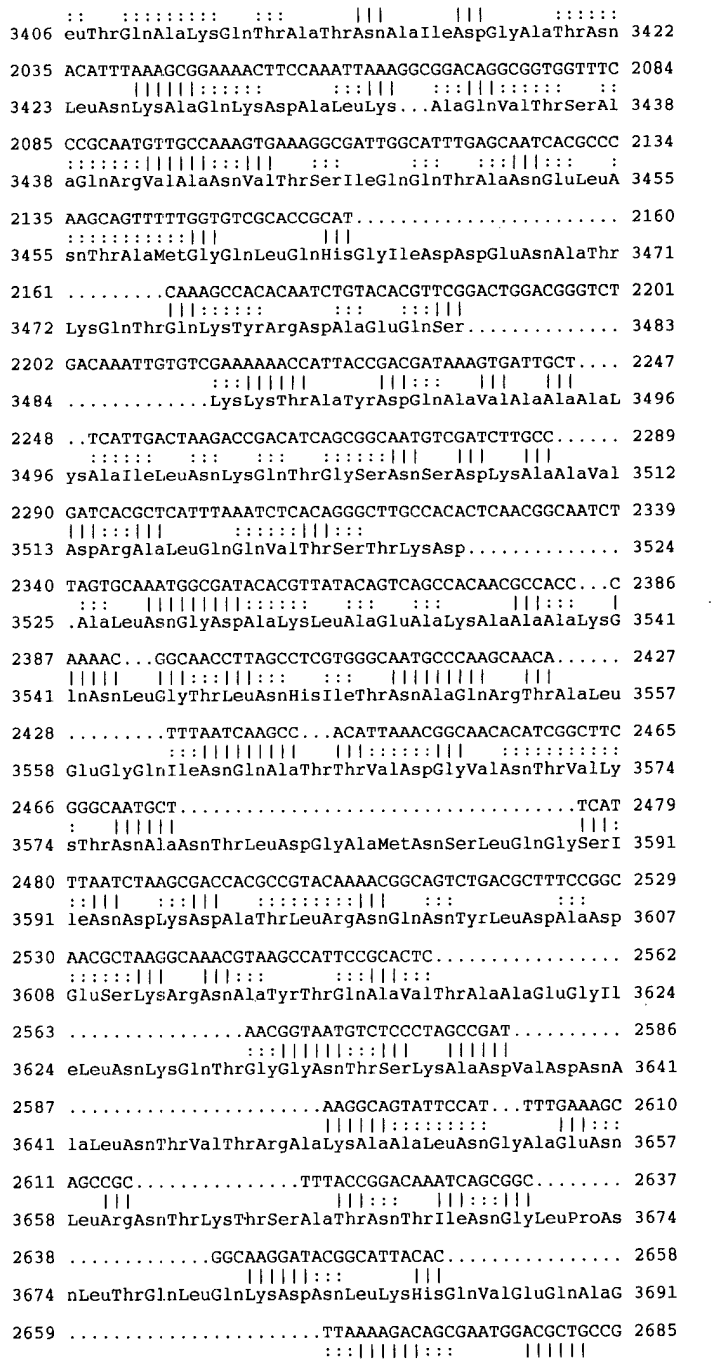
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4116 nAlaTyrAspGluLysValThrAlaAlaGluAsnIleValSerGlyThrP 4133

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seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2001.DAT:AAU37403

seq_documentation_block:
ID AAU37403 standard; Protein; 6281 AA.
XX
AC AAU37403;
XX
DT 14-FEB-2002 (first entry)
XX
DE Staphylococcus aureus cellular proliferation protein #1573.
XX
KW Antisense; prokaryotic cellular proliferation protein;

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KW   antibiotic; antibacterial; drug design.
XX
OS   Staphylococcus aureus.
XX
PN   WO200170955-A2.
XX
PD   27-SEP-2001.
XX
PF   21-MAR-2001; 2001WO-US09180.
XX
PR   21-MAR-2000; 2000US-191078P.
PR   23-MAY-2000; 2000US-206848P.
PR   26-MAY-2000; 2000US-207727P.
PR   23-OCT-2000; 2000US-242578P.
PR   27-NOV-2000; 2000US-253625P.
PR   22-DEC-2000; 2000US-257931P.
PR   16-FEB-2001; 2001US-269308P.
XX
PA   (ELIT-) ELITRA PHARM INC.
XX
PI   Haselbeck R,  Ohlsen KL,  Zyskind JW,  Wall D,  Trawick JD,  Carr GJ;
PI   Yamamoto RT,  Xu HH;
XX
DR   WPI; 2001-611495/70.
DR   N-PSDB; AAS55262.
XX
PT   New polynucleotides for the identification and development of
PT   antibiotics, comprise sequences of antisense nucleic acids -
XX
PS   Example 3; Seq ID No 12996; 511pp; English.
XX
CC   The invention relates to antisense inhibitors of genes essential to
CC   prokaryotic cellular proliferation, their use in identifying the
CC   genes, their use in the discovery of novel antibiotics, the essential
CC   genes themselves and the encoded proteins. The prokaryotes used are
CC   Escherichia coli, Staphylococcus aureus, Salmonella typhi, Klebsiella
CC   pneumoniae, Pseudomonas aeruginosa and Enterococcus faecalis. The
CC   invention is also useful for the identification of potential new targets
CC   for antibiotic development. The antisense nucleic acids can also be used
CC   to identify proteins used in proliferation, to express these proteins,
CC   and to obtain antibodies capable of binding to the expressed proteins.
CC   The proteins can be used to screen compounds in rational drug discovery
CC   programmes. The antisense nucleic acid sequence is also useful to screen
CC   for homologous nucleic acids which are required for cell proliferation in
CC   a wide variety of organisms. The present sequence represents an
CC   essential prokaryotic cellular proliferation protein.
CC   Note: The sequence data for this patent did not form part
CC   of the printed specification, but was obtained in electronic
CC   format directly from WIPO at
CC   ftp.wipo.int/pub/published_pct_sequences.
XX
SQ   Sequence   6281 AA;


alignment_scores:
           Quality:  262.50              Length:   1488
             Ratio:  0.382                 Gaps:     66
 Percent Similarity:  46.237   Percent Identity: 19.825

alignment_block:
 US-09-303-518D-649 x AAU37403   ..

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     457 CATCCTTATGGCGGCGATTATCATATGCCGCGTTTGCATAAATTTGTCAC 506
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     277 laAsnLeuGlnAsnGlyIleAsnAspLysThrAsnThrLeuAlaSerGlu 293

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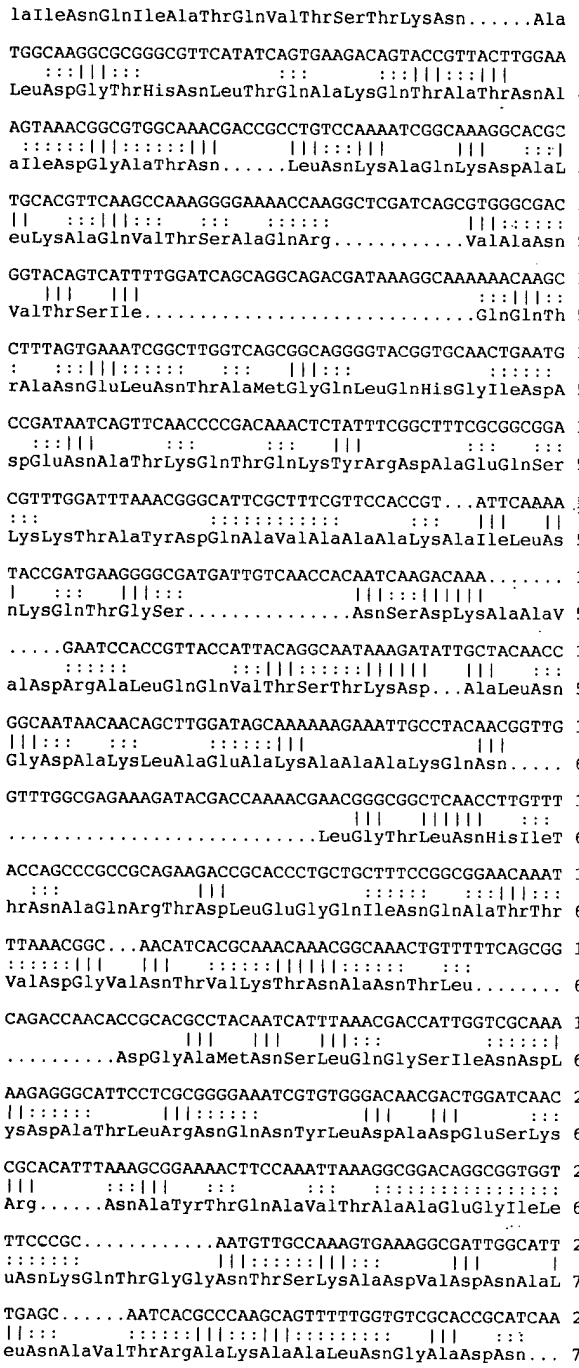
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554 LysLysThrAlaTyrAspGlnAlaValAlaAlaAlaLysAlaIleLeuAs 570
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570 nLysGlnThrGlySer.....AsnSerAspLysAlaAlaV 582
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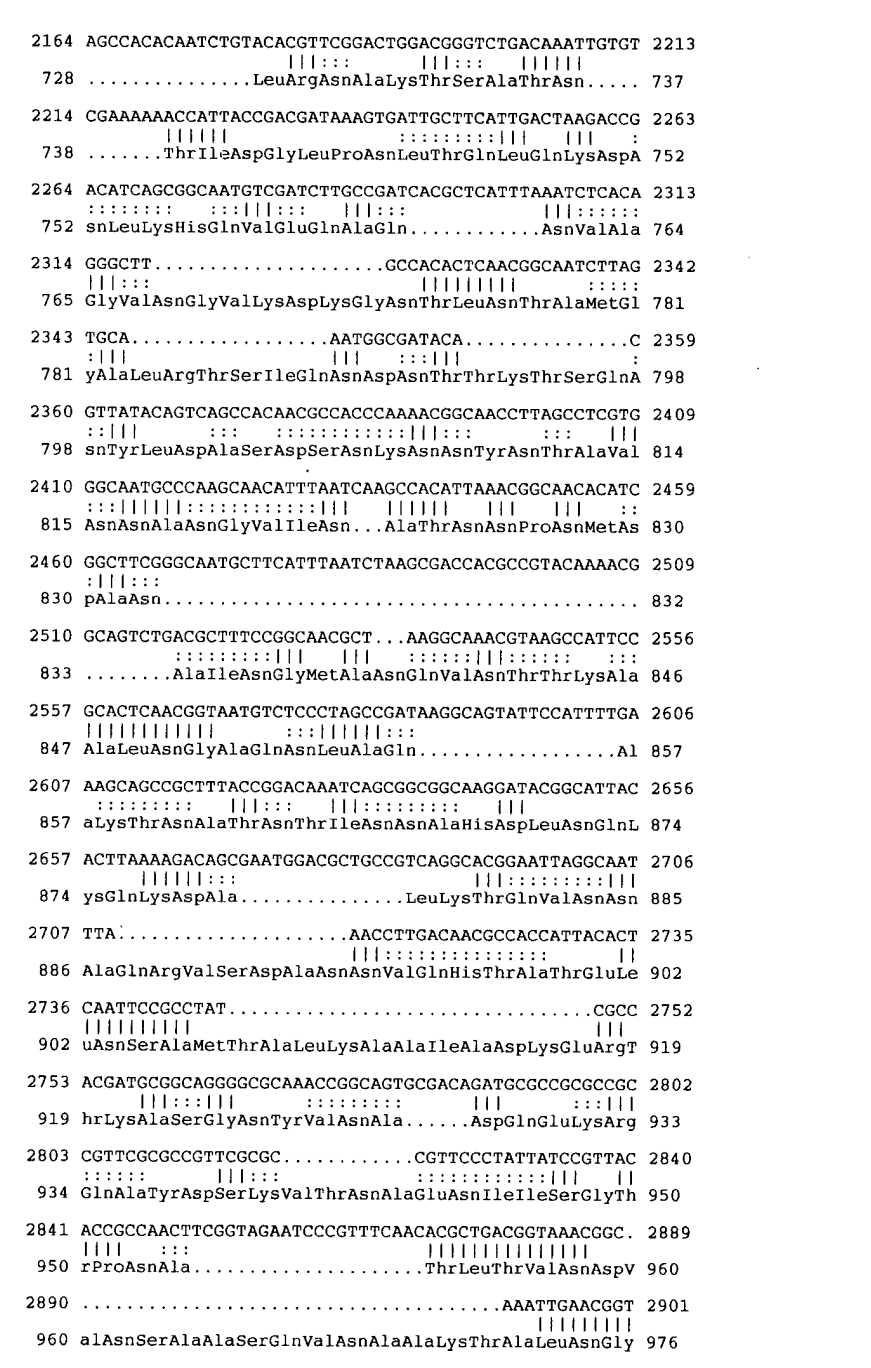
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2314 GGGCTT.....GCCACACTCAACGGCAATCTTAG 2342
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2343 TGCA.....AATGGCGATACA.....C 2359
781 yAlaLeuArgThrSerIleGlnAsnAspAsnThrThrLysThrSerGlnA 798
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950 rProAsnAla.....ThrLeuThrValAsnAspV 960
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2950 .........................AAATTGAAGCTGGCGGAAAGTTCCG 2974
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2975 AAGGCACTTACACCTTG............GCGGTCAACAATACC...... 3006
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3136 ATCCGCAAAGACGGCGAGTTCCGCCTGCATAATCCG.............,... 3171
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3172 ............................GTCAAAGAACAAGAGCTTT 3190
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3291 GACAGAAAGCGTT..................................... 3303
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3303 ..... 3303

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3304 ..........................................GCCGA 3308
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3361 GAGAAAAAACGGGTGCAGGCGGATAAAGACACCGCCTTG.........GC 3401
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     ||   :::   :::|||:::|||:::      |||
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3487 CCCCAACCGCAGCCCCAACCGCAGCGCGACCTGATCAGCCGTTATGCCAA 3536
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1454 hrProThrProThrLeuThrProAlaAspValThrAsnAlaAlaThrGln 1470

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     :::   ::::::
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seq_documentation_block:

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ID   AAU37120 standard; Protein; 2344 AA.
XX
AC   AAU37120;
XX
DT   14-FEB-2002  (first entry)
XX
DE   Staphylococcus aureus cellular proliferation protein #1290.
XX
KW   Antisense; prokaryotic cellular proliferation protein;
KW   antibiotic; antibacterial; drug design.
XX
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OS Staphylococcus aureus.
XX
PN WO200170955-A2.
XX
PD 27-SEP-2001.
XX
PF 21-MAR-2001; 2001WO-US09180.
XX
PR 21-MAR-2000; 2000US-191078P.
PR 23-MAY-2000; 2000US-206848P.
PR 26-MAY-2000; 2000US-207727P.
PR 23-OCT-2000; 2000US-242578P.
PR 27-NOV-2000; 2000US-253625P.
PR 22-DEC-2000; 2000US-257931P.
PR 16-FEB-2001; 2001US-269308P.
XX
PA (ELIT-) ELITRA PHARM INC.
XX
PI Haselbeck R, Ohlsen KL, Zyskind JW, Wall D, Trawick JD, Carr GJ;
PI Yamamoto RT, Xu HH;
XX
DR WPI; 2001-611495/70.
DR N-PSDB; AAS54979.
XX
PT New polynucleotides for the identification and development of
PT antibiotics, comprise sequences of antisense nucleic acids -
XX
PS Example 3; Seq ID No 12713; 511pp; English.
XX
CC The invention relates to antisense inhibitors of genes essential to
CC prokaryotic cellular proliferation, their use in identifying the
CC genes, their use in the discovery of novel antibiotics, the essential
CC genes themselves and the encoded proteins. The prokaryotes used are
CC Escherichia coli, Staphylococcus aureus, Salmonella typhi, Klebsiella
CC pneumoniae, Pseudomonas aeruginosa and Enterococcus faecalis. The
CC invention is also useful for the identification of potential new targets
CC for antibiotic development. The antisense nucleic acids can also be used
CC to identify proteins used in proliferation, to express these proteins,
CC and to obtain antibodies capable of binding to the expressed proteins.
CC The proteins can be used to screen compounds in rational drug discovery
CC programmes. The antisense nucleic acid sequence is also useful to screen
CC for homologous nucleic acids which are required for cell proliferation in
CC a wide variety of organisms. The present sequence represents an
CC essential prokaryotic cellular proliferation protein.
CC Note: The sequence data for this patent did not form part
CC of the printed specification, but was obtained in electronic
CC format directly from WIPO at
CC ftp.wipo.int/pub/published_pct_sequences.
XX
SQ Sequence 2344 AA;

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           Quality:  261.50              Length:   1559
             Ratio:  0.361                Gaps:     58
 Percent Similarity:  46.504   Percent Identity: 17.704

alignment_block:
 US-09-303-518D-649 x AAU37120   ..

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      20 ArgLeuTyrLysSerGlyLysAsnTrpValLysSerGlyIleLysGluIl 36

     213 TGAGGTTTACAACAAAAAAGGGGAGTTGGTCGGCAAATCAATGACAAAAG 262
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      36 eGluMetPheLysIleMetGly.........................L 44

     263 CCCCGATGATTGATTTTTCTGTGGTGTCGCGTAACGGC..... 300
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      44 euProPheIleSerHisSerMetValSerGlnAspAsnGlnSerIleSer 60

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      61 LysLysMetThrGlyTyrGlyLeuLysThrThrAlaValIleGlyGlyAl 77

     324 ATATATTGTGAGCGTGGCACATAAC..... 348
          :::   |||:::::::   |||:::
      77 aPheThrValAsnMetLeuHisAspGlnGlnAlaPheAlaAlaSerAspA 94

     349 ..........................................GGCGGCTAT 357
                                                 |||:::
      94 laProLeuThrSerGluLeuAsnThrGlnSerGluThrValGlyAsnGln 110

     358 AACAACGTTGATTTTGGTGCGGAAGGAAGAAATCCCGAT..... 396
         |||::::::   :::   |||:::      :::   |||
     111 AsnSerThrThrIleAspAlaSerThrSerThrAlaAspSerThrSerVa 127

     397 ..........................CAACATCGTTTTACTTATAAAA 418
                                    ::::::      |||   :::
     127 lThrLysAsnSerSerSerValGlnThrSerAsnSerAspThrValSerS 144

     419 TTGTGAAACGGAATAATTATAAAGCAGGGACTAAAGGCCATCCTTATGGC 468
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     144 erGluLysSerGluAsnValThrSerThrThrAsnSer..... 156

     469 GGCGATTATCATATGCCGCGTTTGCATAAATTTGTCACAGATGCAGAACC 518
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     157 ................................ThrSerAsnGlnGl 161

     519 TGTTGAAATGACCAGTTATATGGATGGGCGGAAATATATCGATCAAAATA 568
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     569 ATTACCCTGACCGTGTTCGTATTGGGGCAGGCAGGCAATATTGGCGATCT 618
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     190 SerThrGluGlnProIleAsnThrSerThrAsnGlnSerThrAlaSerAs 206

     666 ..... 666

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     667 ..................................GCGTATTCTTGG 678
                                           ::::::|||
     223 erThrThrSerThrSerThrAlaProValLysLeuArgThrPheSerArg 239

     679 CTCGTTGGTGGCAATACCTTTGCACAAAATGGATCA.....GG 716
         |||   :::   :::||||||||||:::   ::::::
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     717 TGGTGGCACAGTCAACTTAGGTAGTGAAAAAATTAAACATAGCCCATATG 766
          ::::::|||:::::::::::::::::::::::::|||:::
     255 rAlaAsnThrIleThrValAsnLysAspAsnLeuLysGln..... 268

     767 GTTTTTTACCAACAGGAGGCTCATTT.....GGCGACAGTGGCTCA 807
           ::::::   |||:::|||:::              ::::::|||
     269 ..TyrMetThrThrSerGlyAsnAlaThrTyrAspGlnSerThrGlyVal 284

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     285 ValThrLeuThrGlnAspThrThrSerGlnLysGlyAlaIleThrLeuGl 301

     850 ................................AATGGGGTATTGCAAA 865
                                          :::|||   ::::::
     301 yThrArgIleAspSerAsnLysSerPheHisPheSerGlyLysValAsnL 318

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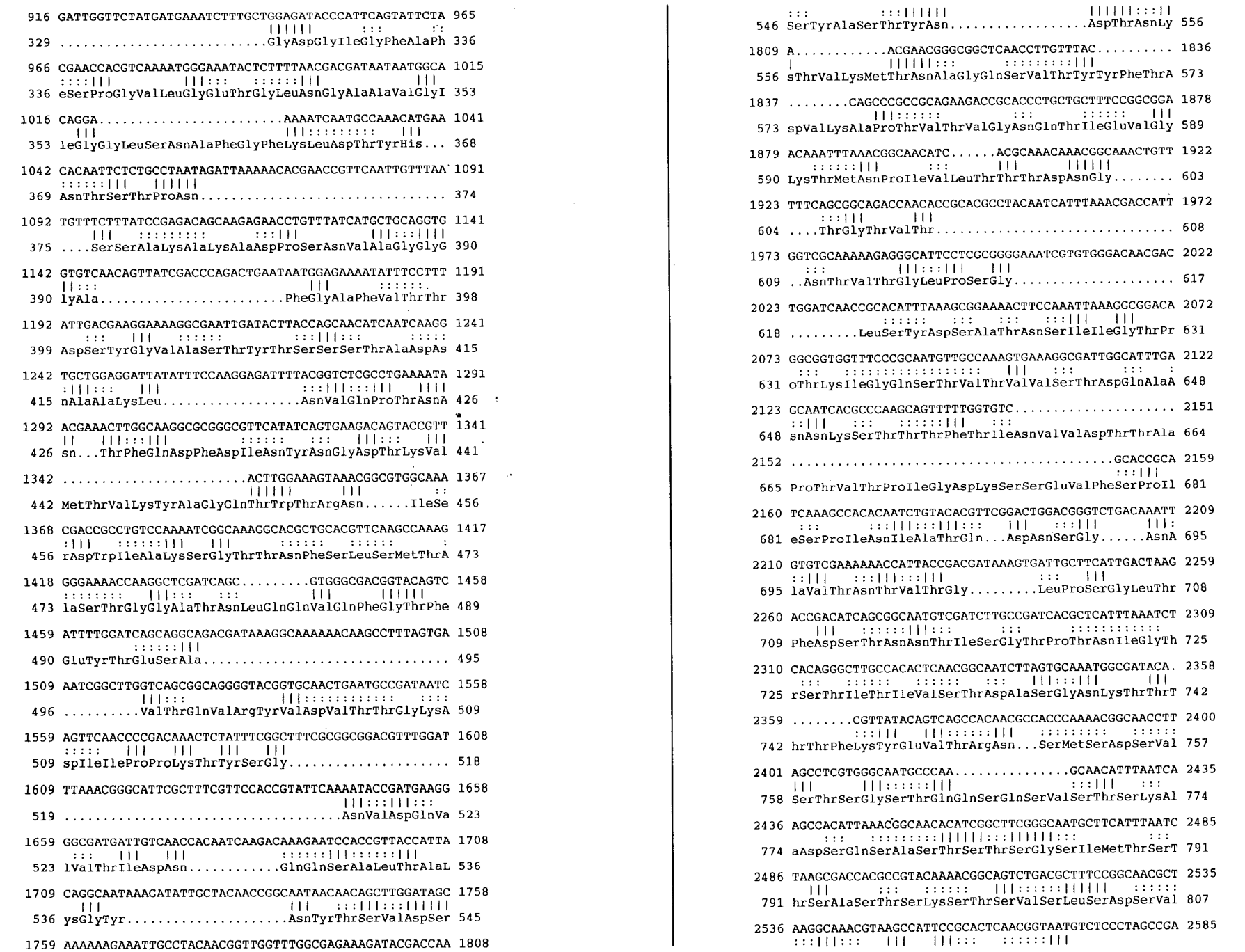


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840 SerGlySerValSerLysSerThrSerLeuSerAspPheIleSerAsnSe 856
2736 CAATTCCGCCTATCGCCACGATGCGGCAGGGGCGCAAACCGGC 2778
856 rSerSerThrGluLysSerGluSerValSerThrSerThrSerAspSerL 873
2779 AGTGCGACAGATGCGCCGCGCCGCCGTTCGCGCCGT 2814
873 euArgThrSerThrSerLeuSerAspSerValSerMetSerThrSerGly 889
2815 TCGCGCCGTTCCCTATTATCCGTTACACCGCCAACTTCGGTAGAATCCCG 2864
890 SerLeuSerLysSerGlnSerLeuSerThrSerThrSerAspSerAlaSe 906
2865 TTTCAACACGCTGACGGTAAACGGCAAATTGAACGGTCAGGGAACATTCC 2914
906 rThrSerGlnSerValSerAspSerThrSerAsnSerIleSerThrSerG 923
2915 GCTTTATGTCGGAACTCTTCGGCTACCGCAGCGACAAATTGAAGCTGGCG 2964
923 luSerLeuSerGlu...SerGlySerThrSerGluSerIleSerIleSer 938
2965 GAAAGTTCCGAAGGCACTTACACCTTGGCGGTCAACAATACCGGCAACGA 3014
939 AsnSerIleSerAsnSerValSerAlaSerThrSerLysLeuGluSerGl 955
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3853 GACAGGTTCTACATCGGCATCAGCGCGGGCGCGGGTT 3889
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1221 uSerThrSerGluSerLeuSerGlySerThrSerAspSerThrSerLeuS 1238
4026 CG TCCAAAAAGCGGATTACCGCTACGAAAACGTCAATATCG 4066
1238 erAspSerAsnSerGluSerGlySerThrSerThrSerLeuSerAsnSer 1254
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1255 ThrSerGlySerAlaSerIleSerThrSerThrSerGlySerAlaSerTh 1271
4102 GGCATTAAGGCAGATTATTCATTCAAACCGG 4132
1271 rSerThrValLysSerGluSerValSerThrSerLeuSerThrSerThrS 1288
4133 CGCAACACATTTCCATCACGCCTTATTTGAGCCTGTCCTATACCGATGCC 4182
1288 erThrSerLeuSerAspSerThrSerLeuSerThrSerLeuSerAspSer 1304
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1305 ThrSerGlySerLysSerAsnSerLeuSerAlaSerMetSerThrSerAs 1321
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seq_documentation_block:
ID   AAB01843 standard; Protein; 992 AA.
XX
AC   AAB01843;
XX
DT   11-SEP-2000  (first entry)
XX
DE   Haemophilus influenzae strain 15 mature HMW1A protein, SEQ ID NO:61.
XX
KW   Mature HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW   non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW   recombinant production; Escherichia coli; antibacterial; vaccine;
KW   human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW   detection; diagnosis.
XX
OS   Haemophilus influenzae strain 15.
XX
PN   WO200020609-A2.
XX
PD   13-APR-2000.
XX
PF   07-OCT-1999;   99WO-CA00938.
XX
PR   07-OCT-1998;   98US-0167568.
PR   08-DEC-1998;   98US-0206942.
XX
PA   (CONN-) CONNAUGHT LAB LTD.
XX
PI   Loosmore SM,  Yang Y,  Klein MH;
XX
DR   WPI; 2000-303789/26.
DR   N-PSDB; AAA52192.
XX
PT   Nucleic acid molecule for producing recombinant high molecular weight
PT   proteins of Haemophilus which are used as a vaccine to provide
PT   protection against Haemophilus induced diseases in humans -
XX
PS   Claim 8; Fig 26A-O; 307pp; English.
XX
CC   The invention relates to the recombinant production of Haemophilus
CC   influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC   expression construct used to effect recombinant expression comprises a
CC   promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC   to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC   influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC   clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC   hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC   and the hmwB and hmwC genes encode accessory proteins which are
CC   responsible for post-translational processing and secretion of the HMWA
CC   proteins. The modified hmwABC operon used in the expression construct of
CC   the invention contains an A gene modified such that it encodes only the
CC   mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC   and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC   strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC   vectors are used for the production of recombinant H. influenzae HMW
CC   proteins which can be used as vaccines to mediate a humoral or
CC   cell-mediated immune response to provide protection against diseases in
CC   humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC   pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC   antigens in immunoassays for detecting antibodies against Haemophilus,
CC   HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC   HMW proteins can be used to isolate and clone hmw genes from other
CC   non-typeable strains of Haemophilus via hybridisation reactions. The
CC   present sequence represents a mature HMWA protein from a non-typeable
CC   strain of H. influenzae.
XX
SQ   Sequence   992 AA;


alignment_scores:
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 Percent Similarity:  47.241   Percent Identity: 19.914

alignment_block:
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           |||   ::::::   |||:::   :::|||::::::
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     684 .............................................. 684

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     684 .............................................. 684

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                                     |||   ||||||:::|||:::
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     754 CATAGCCCATATGGTTTTTTACCAACAGGAGGCTCATTTGGCGACAGTGG 803
         ::::::      :::   :::   :::   |||:::::::   :::::||
     146 AsnAlaSerSerAlaGlnIleThrAlaGlnGlyThrIleThrAsnThrGl 162

     804 CTCACCAATGTTTATCTATGATGCCCAAAAGCAAAAGTGGTTA....... 846
         |:::                        |||||||||      |||
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     847 .....ATTAATGGGGTATTGCAAACGGGCAACCCCTATATAGGAAAAAGC 891
              |||||||||          ||||||      ||||||   :::
     172 alSerIleAsnGly.........ThrGly.........IleGlyLeuAsn 182

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     182 .............................................. 182

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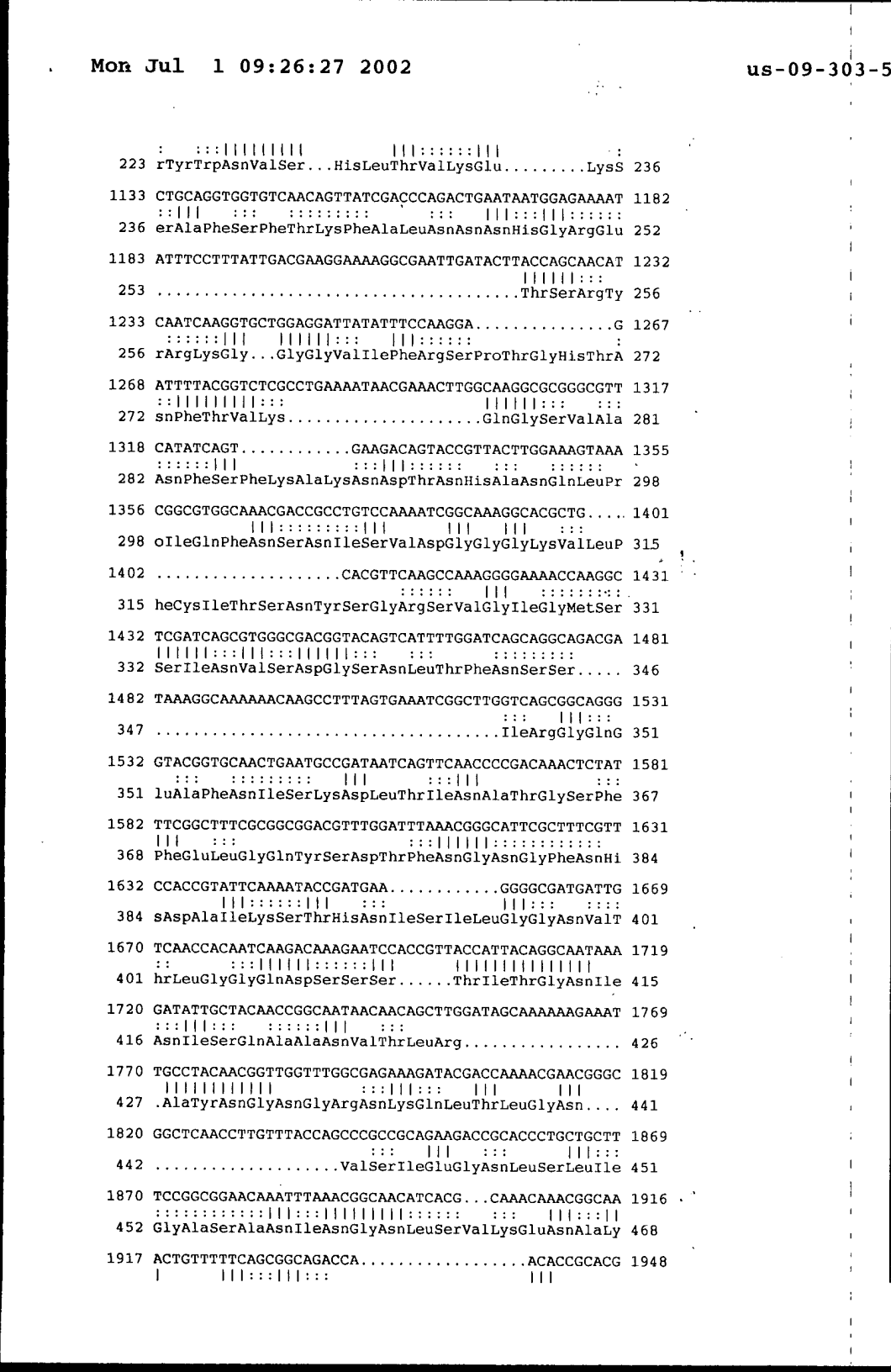
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468 s.....PheLysGlyGluThrGlnAspAsnLeuAsnIleThrGlyThrP 483
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483 heIleAsnAsnGlyAspSerLysIleAsnIleSerGlnGlyValValLys 499
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  812 ........................LeuThrThrValGluGlySerAsnIl 820

 2856 AGAATCCCGTTTCAACACGCTGACGGTAAACGGCAAATTGAACGGTCAGG 2905
      :::::::      :::|||||||::::::|||:::|||
  820 eAsnAlaAlaSerGlyThrLeuValIleAsnAlaLys.............  832

 2906 GAACATTCCGCTTTATGTCGGAACTCTTCGGCTACCGCAGCGACAAATTG 2955
                                              :::   ||||||
  833 ....................................AspAlaLysLeu 836

 2956 AAGCTGGCGGAAAGTTCCGAAGGCACTTACACCTTGGCGGTCAACAATAC 3005
      :::   |||   |||::::::   |||   :::   |||:::|||   ::
  837 AsnGlyAlaAlaSerGlyAspHisThrValValAsnAlaThrAsnAlaSe 853

 3006 CGGCAACGAACCTGCAAGCCTCGAACAATTGACGGTAGTGGAAGGAAAAG 3055
      :|||:::                                    |||:::
  853 rGlySer.................................GlySerV 858

 3056 ACAACAAACCGCTGTCCGAAAACCTTAATTTCACCCTGCAAAACGAACAC 3105
        :::         |||:::|||:::|||:::|||   :::   :::
  858 alThrAlaValThrSerSerAsnValAsnIleThrGlyAspLeuSerThr 874

 3106 GTCGATGCCGGCGCGTGGCGTTACCAACTCATCCGCAAAGACGGCGAGTT 3155
      |||::::::                 :::::::|||   |||:::|||
  875 ValAsnGly............LeuAsnIleIleSerLysAsnGly..... 885

 3156 CCGCCTGCATAATCCGGTCAAAGAACAAGAGCTTTCCGACAAACTCGGCA 3205
             :::|||   |||                            |||
  886 .......ArgAsnThrVal.....................ValLeuLysG 893

 3206 AGGCAGAAGCCAAAAAACAGGCGGAAAAAGACAACGCGCAAAGCCTTGAC 3255
        :::|||   :::   :::      :::   ::::::   |||::::::
  893 lyThrGluIleGluValLysTyrIleGlnProGlyValAlaSerValGlu 909

 3256 GCGCTGATTGCGGCCGGGCGCGATGCCGTCGAAAAGACAGAAAGCGTTGC 3305
         :::|||   |||   |||   ::::::||||||:::::::::::::
  910 GluValIleGluAlaLysArg...ValLeuGluLysValLysAspLeuSe 925

 3306 CGAACCGGCCCGGCAGGCAGGCGGGGAAAATGTCGGCATTATGCAGGCGG 3355
      ::::      |||::::::   ::::::   :::|||:::      :::
  925 rAspGluGluArgGluThrLeuAlaLys...LeuGlyValSerAlaVal. 940

 3356 AGGAAGAGAAAAAACGGGTGCAGGCGGATAAAGACACCGCCTTGGCGAAA 3405
                 :::   ::::::   ::::::      ::::::
  941 ...........ArgPheIleGluProAsnAsnThrIleThrValAsnThr 953

 3406 CAGCGCGAAGCGGAAACCCGGCCGGCTACC 3435
      |||:::|||      |||||||||:::::
  954 GlnAsnGluPheThrThrArgProSerSer 963
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seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2000.DAT:AAB01842

seq_documentation_block:

ID AAB01842 standard; Protein; 998 AA.

XX
AC AAB01842;
XX
DT 11-SEP-2000 (first entry)
XX
DE Haemophilus influenzae strain 15 HMW1A protein, SEQ ID NO:59.
XX
KW HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW recombinant production; Escherichia coli; antibacterial; vaccine;
KW human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW detection; diagnosis.
XX
OS Haemophilus influenzae strain 15.
XX
PN WO200020609-A2.
XX
PD 13-APR-2000.
XX
PF 07-OCT-1999; 99WO-CA00938.
XX
PR 07-OCT-1998; 98US-0167568.
PR 08-DEC-1998; 98US-0206942.
XX
PA (CONN-) CONNAUGHT LAB LTD.
XX
PI Loosmore SM, Yang Y, Klein MH;
XX
DR WPI; 2000-303789/26.
DR N-PSDB; AAA52191.
XX
PT Nucleic acid molecule for producing recombinant high molecular weight
PT proteins of Haemophilus which are used as a vaccine to provide
PT protection against Haemophilus induced diseases in humans -
XX
PS Claim 12; Fig 26A-O; 307pp; English.
XX
CC The invention relates to the recombinant production of Haemophilus
CC influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC expression construct used to effect recombinant expression comprises a
CC promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC and the hmwB and hmwC genes encode accessory proteins which are
CC responsible for post-translational processing and secretion of the HMWA
CC proteins. The modified hmwABC operon used in the expression construct of
CC the invention contains an A gene modified such that it encodes only the
CC mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC vectors are used for the production of recombinant H. influenzae HMW
CC proteins which can be used as vaccines to mediate a humoral or
CC cell-mediated immune response to provide protection against diseases in
CC humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC antigens in immunoassays for detecting antibodies against Haemophilus,
CC HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC HMW proteins can be used to isolate and clone hmw genes from other
CC non-typeable strains of Haemophilus via hybridisation reactions. The
CC present sequence represents an HMWA protein from a non-typeable strain of
CC H. influenzae.
XX
SQ Sequence 998 AA;

alignment_scores:

Quality:	261.00	Length:	1160
Ratio:	0.476	Gaps:	58
Percent Similarity:	47.241	Percent Identity:	19.914

alignment_block:

US-09-303-518D-649 x AAB01842 ..

Align seg 1/1 to: AAB01842 from: 1 to: 998

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  24 eAsp...SerGluPheProGly............GlySerGlyThrLysG 36

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  36 luSerProLysThrAsnGlyGluGlnProThrValLeuThrAsnGluThr 52

 646 AGTTCATATCATATTGCAAGTGCGTATTCTTGGCTCGTT........... 684
        |||   ::::::   |||:::   :::|||::::::       :
  53 IleSerAsnTyrLeuLysSerGly...ThrTrpValMetAsnIleThrAl 68

 684 ..................................................... 684

  68 aLysLysAsnLeuThrValAsnSerSerIleAsnIleGlyAspSerSerH 85

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  85 isLeuIleLeuHisSerGluGlyLysAsnAsnGlyGlyValLysIleLys 101

 685 .................GGTGGCAATACCTTTGCACAAAATGGATCA.. 714
                     |||||||||         |||:::|||:::
 102 GluAspIleThrSerAsnGlyGlyAsnLeuThrIleGlnSerGlyGlyTr 118

 715 ........................GGTGGTGGCACAGTCAACTTA. 735
                            |||   ||||||:::|||::: 
 118 pValAspValHisLysAsnIleThrLeuGlyThrGlyThrLeuAsnIleT 135

 736 ............................GGTAGTGAAAAAATTAAA 753
                                ||||:::||||||   :::
 135 hrAlaLysGlySerIleAlaPheGluGlyAsnGlyThrGluLysAlaArg 151

 754 CATAGCCCATATGGTTTTTTACCAACAGGAGGCTCATTTGGCGACAGTGG 803
     ::::::      :::   :::   :::   |||::::::   :::::::||
 152 AsnAlaSerSerAlaGlnIleThrAlaGlnGlyThrIleThrAsnThrGl 168

 804 CTCACCAATGTTTATCTATGATGCCCAAAAGCAAAAGTGGTTA....... 846
     |:::                  |||||||||      |||
 168 yAsp.....................GlnLysGlnLeuArgLeuAsnAsnV 178

 847 .....ATTAATGGGGTATTGCAAACGGGCAACCCCTATATAGGAAAAAGC 891
          |||||||||         ||||||         ||||||   :::
 178 alSerIleAsnGly.........ThrGly.........IleGlyLeuAsn 188

 892 AATGGCTTCCAGCTGGTTCGTAAAGATTGGTTCTATGATGAAATCTTTGC 941

 188 ..................................................... 188

 942 TGGAGATACCCATTCAGTATTCTACGAACCACGTCAAAATGGGAAATACT 991
                      |||   :::   :::   |||   ::::::
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       |||:::   :::         :::|||::::::         |||
 199 rgPheAspGlyGluLeuIleIleSerGlyArgVal.........HisVal 212

1042 CACAATTCTCTGCCTAATAGATTA.........AAAACACGAACCGTTCA 1082
     :::::::::   |||:::::::|||         |||:::         ::
 213 AsnGlnThrThrProLysAsnLeuSerPheTrpLysValSerAspGluSe 229

1083 ATTGTTTAATGTTTCTTTATCCGAGACAGCAAGAGAACCTGTTTATCATG 1132
     :   :::|||||||||         |||:::::::|||           :
 229 rTyrTrpAsnValSer...HisLeuThrValLysGlu.........LysS 242

1133 CTGCAGGTGGTGTCAACAGTTATCGACCCAGACTGAATAATGGAGAAAAT 1182
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     ::|||   :::   :::::::::      :::   |||:::|||::::::
 242 erAlaPheSerPheThrLysPheAlaLeuAsnAsnAsnHisGlyArgGlu 258

1183 ATTTCCTTTATTGACGAAGGAAAAGGCGAATTGATACTTACCAGCAACAT 1232
                                                |||||||:::
 259 .....................................ThrSerArgTy 262

1233 CAATCAAGGTGCTGGAGGATTATATTTCCAAGGA.............G 1267
       ::::::|||   ||||||:::   |||::::::           :
 262 rArgLysGly...GlyGlyValIlePheArgSerProThrGlyHisThrA 278

1268 ATTTTACGGTCTCGCCTGAAAATAACGAAACTTGGCAAGGCGCGGGCGTT 1317
     ::||||||||||:::                     ||||||:::   :::
 278 snPheThrValLys.....................GlnGlySerValAla 287

1318 CATATCAGT............GAAGACAGTACCGTTACTTGGAAAGTAAA 1355
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 288 AsnPheSerPheLysAlaLysAsnAspThrAsnHisAlaAsnGlnLeuPr 304

1356 CGGCGTGGCAAACGACCGCCTGTCCAAAATCGGCAAAGGCACGCTG.... 1401
               |||::::::::::|||      |||   |||   :::
 304 oIleGlnPheAsnSerAsnIleSerValAspGlyGlyGlyLysValLeuP 321

1402 ...................CACGTTCAAGCCAAAGGGGAAAACCAAGGC 1431
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 321 heCysIleThrSerAsnTyrSerGlyArgSerValGlyIleGlyMetSer 337

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 338 SerIleAsnValSerAspGlySerAsnLeuThrPheAsnSerSer..... 352

1482 TAAAGGCAAAAAACAAGCCTTTAGTGAAATCGGCTTGGTCAGCGGCAGGG 1531
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 353 ..................................IleArgGlyGlnG 357

1532 GTACGGTGCAACTGAATGCCGATAATCAGTTCAACCCCGACAAACTCTAT 1581
       :::   :::::::::   |||      :::|||            :::
 357 luAlaPheAsnIleSerLysAspLeuThrIleAsnAlaThrGlySerPhe 373

1582 TTCGGCTTTCGCGGCGGACGTTTGGATTTAAACGGGCATTCGCTTTCGTT 1631
     |||   :::                  :::|||||||::::::::::
 374 PheGluLeuGlyGlnTyrSerAspThrPheAsnGlyAsnGlyPheAsnHi 390

1632 CCACCGTATTCAAAATACCGATGAA............GGGGCGATGATTG 1669
            |||:::::::|||   :::             |||:::   ::::
 390 sAspAlaIleLysSerThrHisAsnIleSerIleLeuGlyGlyAsnValT 407

1670 TCAACCACAATCAAGACAAAGAATCCACCGTTACCATTACAGGCAATAAA 1719
     ::       :::||||||::::::|||       ||||||||||||||
 407 hrLeuGlyGlyGlnAspSerSerSer......ThrIleThrGlyAsnIle 421

1720 GATATTGCTACAACCGGCAATAACAACAGCTTGGATAGCAAAAAAGAAAT 1769
     :::|||:::   :::::::|||   :::
 422 AsnIleSerGlnAlaAlaAsnValThrLeuArg................. 432

1770 TGCCTACAACGGTTGGTTTGGCGAGAAAGATACGACCAAAACGAACGGGC 1819
      ||||||||||||         :::|||:::   |||      |||
 433 .AlaTyrAsnGlyAsnGlyArgAsnLysGlnLeuThrLeuGlyAsn.... 447

1820 GGCTCAACCTTGTTTACCAGCCCGCCGCAGAAGACCGCACCCTGCTGCTT 1869
                                   :::   |||   :::      |||:::
 448 ....................ValSerIleGluGlyAsnLeuSerLeuIle 457

1870 TCCGGCGGAACAAATTTAAACGGCAACATCACG...CAAACAAACGGCAA 1916
     ::::::::::::|||:::||||||||||:::::   :::   |||:::||
 458 GlyAlaSerAlaAsnIleAsnGlyAsnLeuSerValLysGluAsnAlaLy 474

1917 ACTGTTTTTCAGCGGCAGACCA..................ACACCGCACG 1948
     |      |||:::|||:::                        |||
 474 s......PheLysGlyGluThrGlnAspAsnLeuAsnIleThrGlyThrP 489

1949 CCTACAATCATTTAAACGACCATTGGTCGCAAAAAGAGGGCATTCCTCGC 1998
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 489 heIleAsnAsnGlyAspSerLysIleAsnIleSerGlnGlyValValLys 505

1999 ...GGGGAAATCGTGTGGGACAACGACTGGATCAACCGCACATTTAAAGC 2045
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 506 LeuGlyAsnValThrAsnAspGlyAsp...LeuAsnIleThrThrHisAl 521

2046 GGAAAACTTCCAA......ATTAAAGGCGGACAGGCGGTG.......... 2079
     |:::::   |||      |||   ||||||:::   :::
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2080 ..........................................GTTTCC 2085
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2086 CGCAATGTTGCCAAAGTGAAAGGCGATTGG..................... 2115
     |||:::::::::   :::|||:::
 555 GlyAsnIleSerGlnLysGluGlyAsnLeuThrIleSerSerAspLysIl 571

2116 .CATTTGAGCAATCACGCCCAAGCAGTTTTTGGTGTCGCACCGCATCAAA 2164
      :::::::::|||:::          ||||||      ::::::|
 571 eAsnIleThrAsnGlnIleThrIleLysAlaGlyValAspGlyGluAsnS 588

2165 GCCACACAATCTGTACACGTTCGGACTGGACGGGTCTGACAAATTGTGTC 2214
     ||                  ||||||   |||:::   :::|||  :::
 588 erAsp.............SerAspAlaThrAsnAsnAlaAsnLeuThr 599

2215 GAAAAAACC...........ATTACCGACGATAAAGTGATTGCTTCATT 2252
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 600 IleLysThrLysGluLeuLysLeuThrGlnAspLeuAsnIleSerGlyPh 616

2253 GACTAAGACCGACATCAGC.........................GGCA 2275
     ::::|||:::::::|||:::                      ||||
 616 eAsnLysAlaGluIleThrAlaLysAspGlySerAspLeuThrIleGlyA 633

2276 ATGTCGATCTTGCCGATCACGCTCATTTAAATCTCACAGGGCTT...... 2319
     ||::::::   ||||||   ::::::   :::   :::   :::
 633 snThrAsnSerAlaAspSerThrAsnAlaLysLysValThrPheAsnGln 649

2320 ..................................GCCACACTCAACGG 2333
                                       :::|||||||||::
 650 ValLysAspSerLysIleSerAlaGlyAspHisAsnValThrLeuAsnSe 666

2334 CAATCTTAGTGCAAATGGCGATACACGTTATACA.............. 2367
     ::::::::::::::::|||:::|||      |||
 666 rLysValGluThrSerGlyAsnThrAspAsnThrGlyAspGlySerGlyA 683

2368 .....................................GTCAGCCACAAC 2379
                                         |||:::::::|||
 683 snAsnAlaGlyLeuThrIleAlaAlaLysAsnValGluValLysAsnAsn 699

2380 GCCACCCAAAACGGCAACCTTAGCCTCGTGGGCAATGCCCAAGCAACATT 2429
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 700 IleThrSerAsnLysThrValAsnIleThrAlaSerGluLysLeuThrTh 716

2430 TAAT...CAAGCCACATTAAACGGCAACACATCGGCTTCGGGCAATGCTT 2476
      :::   :::||||||:::|||:::::::|||         ||||||::::
 716 rLysAlaAspAlaThrIleAsnAlaThrThr.........GlyAsnValG 730

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2527 GGCAACGCTAAGGCAAACGTAAGCCATTCCGCACTCAAC...GGTAATGT 2573
     ||||||::::::   :::::::::   :::::||||||   :::|||||
 747 GlyAsnValAsnIleThrAlaAsnGlyAspThrLeuAsnValSerAsnVa 763

2574 CTCC.................CTAGCCGATAAGGCAGTATTCCATTTTG 2605
     ||||                 |||||||||:::   :::      :
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2606 AAAGCAGCCGCTTTACCGGACAAATCAGCGGCGGCAAGGATACGGCATTA 2655
     :::::|||      ::::::      |||::::::   :::|||:::|||
 780 lnAlaSer......SerSerIleThrSerAsnAsnGlyGlnThrThrLeu 794

2656 CACTTAAAAGACAGCGAATGGACGCTGCCGTCAGGCACGGAATTAGGCAA 2705
          ||||||                      |||:::      |||::
 795 ThrAlaLysAsp.....................GlySerIleAlaGlySe 804

2706 TTTAAACCTTGACAACGCCACCATTACACTCAATTCCGCCTATCGCCACG 2755
     ::::|||         |||:::::|||||||||:::
 804 rIleAsnAla......AlaAsnValThrLeuAsnThr.............. 814

2756 ATGCGGCAGGGGCGCAAACCGGCAGTGCGACAGATGCGCCGCGCCGCCGT 2805
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 815 .................ThrGlyThr........................ 817

2806 TCGCGCCGTTCGCGCCGTTCCCTATTATCCGTTACACCGCCAACTTCGGT 2855
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 818 .......................LeuThrThrValGluGlySerAsnIl 826

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2906 GAACATTCCGCTTTATGTCGGAACTCTTCGGCTACCGCAGCGACAAATTG 2955
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3006 CGGCAACGAACCTGCAAGCCTCGAACAATTGACGGTAGTGGAAGGAAAAG 3055
     :|||:::                                    |||:::
 859 rGlySer.....................................GlySerV 864

3056 ACAACAAACCGCTGTCCGAAAACCTTAATTTCACCCTGCAAAACGAACAC 3105
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 864 alThrAlaValThrSerSerAsnValAsnIleThrGlyAspLeuSerThr 880

3106 GTCGATGCCGGCGCGTGGCGTTACCAACTCATCCGCAAAGACGGCGAGTT 3155
     |||::::::               ::::::|||   |||:::|||
 881 ValAsnGly............LeuAsnIleIleSerLysAsnGly..... 891

3156 CCGCCTGCATAATCCGGTCAAAGAACAAGAGCTTTCCGACAAACTCGGCA 3205
            :::|||   |||                        |||
 892 .......ArgAsnThrVal.....................ValLeuLysG 899

3206 AGGCAGAAGCCAAAAAACAGGCGGAAAAAGACAACGCGCAAAGCCTTGAC 3255
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3256 GCGCTGATTGCGGCCGGGCGCGATGCCGTCGAAAAGACAGAAAGCGTTGC 3305
       ::::||   |||   |||   ::::::||||||:::::::::::::::
 916 GluValIleGluAlaLysArg...ValLeuGluLysValLysAspLeuSe 931

3306 CGAACCGGCCCGGCAGGCAGGCGGGGAAAATGTCGGCATTATGCAGGCGG 3355
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 931 rAspGluGluArgGluThrLeuAlaLys...LeuGlyValSerAlaVal. 946

3356 AGGAAGAGAAAAAAACGGGTGCAGGCGGATAAAGACACCGCCTTGGCGAAA 3405
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 947 ...........ArgPheIleGluProAsnAsnThrIleThrValAsnThr 959

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     |||:::|||      |||||||||:::::
 960 GlnAsnGluPheThrThrArgProSerSer 969
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seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2000.DAT:AAB01833

seq_documentation_block:

ID AAB01833 standard; Protein; 1005 AA.
XX
AC AAB01833;
XX
DT 11-SEP-2000 (first entry)

XX
DE Haemophilus influenzae strain K21 mature HMW2A protein, SEQ ID NO:41.
XX
KW Mature HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW recombinant production; Escherichia coli; antibacterial; vaccine;
KW human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW detection; diagnosis.
XX
OS Haemophilus influenzae strain K21.
XX
PN WO200020609-A2.
XX
PD 13-APR-2000.
XX
PF 07-OCT-1999; 99WO-CA00938.
XX
PR 07-OCT-1998; 98US-0167568.
PR 08-DEC-1998; 98US-0206942.
XX
PA (CONN-) CONNAUGHT LAB LTD.
XX
PI Loosmore SM, Yang Y, Klein MH;
XX
DR WPI; 2000-303789/26.
DR N-PSDB; AAA52182.
XX
PT Nucleic acid molecule for producing recombinant high molecular weight
PT proteins of Haemophilus which are used as a vaccine to provide
PT protection against Haemophilus induced diseases in humans -
XX
PS Claim 8; Fig 21A-O; 307pp; English.
XX
CC The invention relates to the recombinant production of Haemophilus
CC influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC expression construct used to effect recombinant expression comprises a
CC promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC and the hmwB and hmwC genes encode accessory proteins which are
CC responsible for post-translational processing and secretion of the HMWA
CC proteins. The modified hmwABC operon used in the expression construct of
CC the invention contains an A gene modified such that it encodes only the
CC mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC vectors are used for the production of recombinant H. influenzae HMW
CC proteins which can be used as vaccines to mediate a humoral or
CC cell-mediated immune response to provide protection against diseases in
CC humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC antigens in immunoassays for detecting antibodies against Haemophilus,
CC HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC HMW proteins can be used to isolate and clone hmw genes from other
CC non-typeable strains of Haemophilus via hybridisation reactions. The
CC present sequence represents a mature HMWA protein from a non-typeable
CC strain of H. influenzae.
XX
SQ Sequence 1005 AA;

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Ratio: 0.451 Gaps: 54
Percent Similarity: 49.698 Percent Identity: 20.276

alignment_block:
US-09-303-518D-649 x AAB01833 ..

Align seg 1/1 to: AAB01833 from: 1 to: 1005

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 45 GlnLysGlyIleGluValAsnIleSerAlaThrLysAsnValThrValAs 61

276 TTTTTCTGTGGTGTCGCGTAACGGCGTGGCGGCATTGGTGGGCGATCAAT 325
    :   :::|||      :::|||||||:::   :::|||   :::::::::
 61 nAlaAspValAspValLysAsnGlyThrLeuValLeuHisSerGlnArgA 78

326 ATATTGTGAGCGTGGCACATAACGGCGGCTATAACAACGTTGATTTTGGT 375
       |||::::::      ||||||::: ||||||:::
 78 snGlyValLysIle......AsnGlyAsn.IleThrSerThrGln..... 90

376 GCGGAAGGAAGAAATCCCGATCAACATCGTTTTACTTATAAAATTGTGAA 425
                                                     |
 91 .............................................A 91

426 ACGGA...ATAATTATAAAGCAGGGACTAAAGGCCATCCTTATGGCGGCG 472
    |||||   :::   ||||||   |||   |||:::   :::
 91 snGlyAsnLeuThrIleLysThrGlyGlyLysValAspValHisLysAsn 107

473 ATTATCATATGCCGCGTTTGCATAAATTTGTCACAGATGCAGAACCTGTT 522
    |||   :::            :::|||:::::::::   :::|||:::
108 IleThrLeuGlyMetGlyPheLeuAsnIleThrSerAspAsnAsnIle.. 123

523 GAAATGACCAGTTATATGGATGGGCGGAAATATATCGATCAAAATAATTA 572
              ::::::      |||   |||:::::::|||
124 .........ThrPheGluLysGlyAspAsnLeuThrIleThr..... 134

573 CCCTGACCGTGTTCGTATTGGGGCAGGCAGGCAATATTGGCGATCTGATG 622
                                  |||||||||     |||::::
135 ......................AlaGlnGlyAsnIle..IleSerAsnG 143

623 AAGATGAGCCCAATAACCGCGAAAGTTCATATCATATTGCAAGTGCGTAT 672
    ::::::::   :::   |||   |||:::      :::
143 lnGluAsnLysGlnLeuArgPheSerAsnValSerLeu............ 155

673 TCTTGGCTCGTTGGTGGCAATACCTTTGCACAAAATGGATCAGGT..... 717
    :::   :::   :::|||   ||||||:::   |||   ::::::
156 AsnGlyMetGlyAlaGlyLeuThrPheThrAlaAsnLysGlyAsnHisTh 172

718 ..........GGTGGCACAGTCAACTTAGGTAGTGAAAAAATT......A 751
                |||||||:::|||:::::::::::   :::      :
172 rHisLysPheAspGlyThrLeuAsnIleSerGlyLysValValIleAsnG 189

752 AACATAGCCCATATGGTTTTTTACCAACAGGAGGCTCA..... 789
    ::   :::|||:::::::::   |||   ::::::|||
189 lnThrThrProHisAsnIleAlaProTrpAsnAlaSerAlaAspSerTyr 205

790 ....................TTTGGCGACAGTGGCTCACCAATGTTTAT 818
                        :::|||:::::::::::      |||||
206 TrpAsnValThrThrLeuThrLeuGlyAsnAsnAlaGlnPheThrPheIl 222

819 C......TATGATGCCCAAAAGCAAAAGTGGTTAATTAATGGGGTATTGC 862
    |         |||:::::::::::::      |||   :::|||      :
222 eLysPheValAspSerAsnArgSerValAlaLeuAsnSerGlySerArgS 239

863 AA...ACGGGCAACCCCTATATAGGAAAAAGCAATGGCTTCCAGCTGGTT 909
    ::   :::|||      :::   ||||||:::|||   :::
239 erPheAlaGlyValLysPheTyrGlyLysAsnAsnGluMet......... 252

910 CGTAAAGATTGGTTCTATGATGAAATCTTTGCTGGAGATACCCATTCAGT 959
                        ::::::      |||||||:::   :::||
253 ....................LysPheAsnIleGlyAspAsnAlaAsnVa 262

960 ATTCTACGAACCACGTCAAAATGGGAAATACTCTTTTAACGAC....... 1002
    |   ::::::   ::::::|||   :::   |||   |||
262 lGluPheLysLeuLysSerAsnAspAsnThrSerAsnAsnLysProLeuP 279

1003 ............................GATAATAATGGCACAGGAAAA 1023
                                    :::||||||||||   :::
279 roIleGlnPheLeuSerAsnIleSerAlaThrGlyAsnGlyThrValSer 295

1024 ATCAATGCCAAACATGAACACAATTCTCTGCCTAATAGATTAAAAACACG 1073
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      ::::::            |||   :::|||      |||
  296 PheAspIle.........HisAlaAsnLeuSerAlaArgSerThrGluLe 309

 1074 AACCGTTCAATTGTTTAATGTTTCT........................ 1098
       :::::::::|||:::|||:::|||
  309 uAsnMetSerLeuIleAsnIleSerAsnGlyValAsnPheSerIleAsnS 326

 1099 ...................TTATCCGAGACAGCAAGAGAACCTGTTTAT 1128
                           |||      ::::::   :::
  326 erHisValArgGlyAsnAsnAlaPheGluIleLysLysAspLeuIleIle 342

 1129 CATGCTGCAGGTGGTGTCAACAGTTATCGACCCAGACTGAATAATGGAGA 1178
      :::|||:::|||:::      :::   :::         ::::::   ::
  343 AsnAlaThrGlySerAsnPheAsnLeuLysGlnThrLysAspLysPheAs 359

 1179 AAATATTTCCTTTATTGACGAAGGAAAAGGCGAATTGATACTTACCAGCA 1228
      :|||           :::    |||:::   ::::::   |||   |
  359 pAsn...........SerTyrGluLysAsnAlaIlePheSerThrHisA 372

 1229 ACATCAATCAAGGTGCTGGAGGATTATATTTCCAAGGAGATTTTACGGTC 1278
      ||::::::                    :::   |||:::   |||:::
  372 snLeuThr.................IleLeuGlyGlyAsnValThrLeu 382

 1279 TCGCCTGAAAATAACGAAACTTGGCAAGGCGCGGGCGTTCATATCAGTGA 1328
      :::   ||||||:::::::::       :::::::::::|||:::::
  383 GlyGlyGluAsnSerSerSerAsnIleLysGlyAsnIleAsnIleAsnSe 399

 1329 AGACAGTACCGTTACTTGGAAAGTAAACGGCGTGGCAAACGACCGCCTGT 1378
      :   ::::::||||||   ::::::::::::
  399 rLysAlaAsnValThrLeuGlnAlaHisAla..................... 409

 1379 CCAAAATCGGCAAAGGCACGCTGCACGTTCAAGCCAAAGGGGAA...... 1422
                  ||||||   |||::::::   |||   :::
  410 ..............GlyThrSerHisLeuAspLysLysGluArgThrLeu 421

 1423 AACCAAGGCTCGATCAGCGTGGGCGACGGTACAGTCATTTTGGATCAGCA 1472
      :::   |||:::::::|||||||||   :::       |||:::   :::::
  422 ThrLeuGlyAsnValSerValGlyGlyAsnLeuAsnIleIleGlySerAs 438

 1473 GGCAGACGATAAAGGCAAAAAACAAGCCTTTAGTGAAATCGGCTTGGTCA 1522
      :|||          |||   :::   ::::::::::|||   :::       :
  438 nAlaHisIleAspGly...AsnLeuSerIleAlaGluSerAlaLysPheG 454

 1523 GCGGCAGGGGTACGGTGCAACTGAATGCCGATAATCAGTTCAACCCCGAC 1572
      ::|||:::   :::   :::|||||       :::   |||:::
  454 lnGlyLysThrAsnAsnAsnLeuAsnIleThrGlyThrPheThr...... 468

 1573 AAACTCTATTTCGGCTTTCGCGGCGGACGTTTGGATTTAAACGGGCATTC 1622
                       ::::::|||      |||:::|||
  469 ..................AsnAsnGlyThrAlaAspIleAsn........ 476

 1623 GCTTTCGTTCCACCGTATTCAAAATACCGATGAAGGGGCGATGATTGTCA 1672

  476 ..................................................... 476

 1673 ACCACAATCAAGACAAAGAATCCACCGTTACCATTACAGGCAATAAAGAT 1722
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  477 ..........IleLysGlnGlyValValLysLeuGlnGly......... 486

 1723 ATTGCTACAACCGGCAATAACAACAGCTTGGATAGCAAAAAAGAAATTGC 1772

  486 ..................................................... 486

 1773 CTACAACGGTTGGTTTGGCGAGAAAGATACGACCAAAACGAACGGGCGGC 1822
                            |||   |||   :::||||||:::|
  487 ........................AspIleThr...AsnAsnGlyAsnL 494

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  494 euAsnIleThrThrAsnAlaSerValAsnGlnLysThrIle......... 507

 1873 GGCGGAACAAATTTAAACGGCAACATCACGCAAACAAACGGCAAACTGTT 1922
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  508 ............IleAsnGlyAsnIleThrAsnLysLysGlyAspLeuAs 520

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  520 nIleLysAspIleLysAla...AsnAlaGluIleGlnIleGlyGlyAsnI 536

 1973 GGTCGCAAAAAGAGGGCATTCCTCGCGGGGAAATCGTGTGGGACAACGAC 2022
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  536 leSerGlnLysGlu............GlyAsnLeuThrIleSerSerAsp 548

 2023 TGGATCAACCGCACATTTAAAGCGGAAAACTTCCAAATTAAAGGCGGACA 2072
        ||||||   |||   :::   |||
  549 LysIleAsnIleThrLysArgIleGlu....................... 557

 2073 GGCGGTGGTTTCCCGCAATGTTGCCAAAGTGAAAGGCGATTGGCATTTGA 2122
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  558 ............................IleLysAlaAsp.........T 562

 2123 GCAATCACGCCCAAGCAGTTTTTGGTGTCGCACCGCATCAAAGCCACACA 2172
      ::::::::::::::::       |||||||||   :::   :::   |||
  562 hrAspGlnGlyAsnSerAspSerGlyValAlaSerAsnAlaAsnLeuThr 578

 2173 ATCTGTACACGTTCGGACTGGACGGGTCTGACAAATTGTGTCGAAAAAAC 2222
      |||   |||:::                                  |||   ||
  579 IleLysThrLys............................GluLeuTh 585

 2223 CATTACCGACGATAAAGTGATTGCTTCATTGACTAAGACCGACATCAGCG 2272
      |:::||||||:::       |||:::::::::::::|||:::::|||::::
  585 rLeuThrAspAsnLeuAsnIleSerGlyPheAsnLysAlaGluIleThrA 602

 2273 GC......AATGTCGATCTTGCCGATCACGCTCATTTAAATCTCACAGGG 2316
      ::       |||   ||||||
  602 laLysAspAsnSerAspLeu............................. 608

 2317 CTTGCCACACTCAACGGCAATCTTAGTGCAAATGGCGATACACGTTATAC 2366
                ::::   |||:::   |||:::::::::::::::
  609 .........IleIleGlyLysAlaSerSerAspAsnSerAsnAlaLysGl 622

 2367 AGTCAGCCACAACGCCACCCAAAACGGCAACCTTAGCCTCGTGGGCAATG 2416
       ::::::   :::   ::::::::::::::::::|||   :::||||||
  622 nIleThrPheAspLysValLysAspSerLysIleSer...AlaGlyAsnH 638

 2417 CCCAAGCAACATTTAATCAAGCCACATTAAACGGCAACACATCGGCTTCG 2466
       ::::::|||:::|||:::   :::   :::::::|||:::::::::|||
  638 isAsnValThrLeuAsnSerLysValGluThrSerAsnSerAspGlySer 654

 2467 ...GGCAATGCTTCA..................................... 2478
         ||||||:::|||
  655 ThrGlyAsnGlySerAspAspAsnAsnIleGlyLeuThrIleSerAlaLy 671

 2479 ................TTTAATCTAAGCGACCACGCCGTACAAAACGGCA 2512
                        |||:::::::::|||   :::   |||   |
  671 sAspValThrValAsnSerAsnIleThrSerHisLysThrValAsnIleS 688

 2513 GTCTGACGCTTTCCGGC...AACGCTAAGGCAAACGTAAGCCATTCCGCA 2559
      ||   :::   :::|||   ::::::||||||:::::::::   :::|||
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 2560 CTCAACGGTAATGTCTCCCTAGCCGATAAGGCAGTATTCCATTTTGAAAG 2609
        :::|||:::|||:::::::::   |||
  705 ThrThrGlySerValGluValThrAlaLys..................... 714

 2610 CAGCCGCTTTACCGGACAAATCAGCGGC.........GGCAAGGATACGG 2650
                |||||||:::|||||||||         ||||||   ::::
  715 ..........ThrGlyAspIleSerGlyThrIleSerGlyLysThrValS 728

 2651 CATTACACTTAAAAGACAGCGAATGGACGCTGCCGTCAGGCACGGAATTA 2700
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  728 erValThrAlaThrThrAspSerLeuThrValLysGlyGlyAlaLysIle 744

 2701 GGCAATTTAAACCTTGACAACGCCACCATTACACTCAATTCCGCCTATCG 2750
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  745 ...AsnAlaThrGluGlyThrAlaThrLeuThrAlaSerSerGly..... 758
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 2801 GCCGTTCGCGCCGTTCGCGCCGTTCCCTATTATCCGTTACA..... 2841
         :::      |||:::   :::   :::|||   |||
  773 lyValThrAlaSerSerGlnSerGlyAspIleSerGlyThrIleSerGly 789

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         :::|||||   :::      ::::::|||||||||:::|||
  790 LysThrValSerValThrAlaSerSerGlySerLeuThrValGlyGlyAs 806

 2890 ....AAATTGAACGGT...CAGGGAACATTCCGCTTTATGTCGGAACTCT 2932
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  806 pAlaLysIleAsnAlaThrGluGlyAlaAlaThrLeuThrAlaThrLysG 823

 2933 TCGGCTACCGCAGCGACAAATTGAAGCTGGCGGAAAGTTCCGAAGGCACT 2982
                :::   |||   :::      :::::::::|||||||||
  823 lyThrLeuThrThrValLysGlySerAsnIleAspAlaAsnGluGlyThr 839

 2983 TACACCTTG...GCGGTCAACAATACCGGCAACGAACCTGCAAGCCTCGA 3029
        ::::::   |||   :::   |||   |||      ||||||   ::
  840 LeuValIleAsnAlaGlnAspAlaThrLeuAsnGlyAspAlaSerGlyAs 856

 3030 ACAATTGACGGTA............GTGGAAGGAAAAGACAAC......A 3061
      ::::      |||            ::::::|||:::   |||
  856 pArgThrGluValAsnAlaValAsnAlaSerGlySerGlyAsnValThrA 873

 3062 AACCGCTGTCCGAAAACCTTAATTTCACCCTGCAAAACGAACACGTCGAT 3111
            |||::::::::::|||:::|||   :::   :::   ::::::
  873 laLysThrSerSerSerValAsnIleThrGlyAspLeuSerThrIleAsn 889

 3112 GCCGGCGCGTGGCGTTACCAACTCATCCGCAAAGACGGCGAGTTCCGCCT 3161
      :::               :::::|||   |||:::|||:::
  890 Gly............LeuAsnIleIleSerLysAsnGlyLys........ 899

 3162 GCATAATCCGGTCAAAGAACAAGAGCTTTCCGACAAACTCGGCAAGGCAG 3211
         |||   |||                          |||      ||||
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 3212 AAGCCAAAAAACAGGCGGAAAAAGACAACGCGCAAAGCCTTGACGCGCTG 3261
      ||         :::      :::   ::::::   |||   :::   :::
  908 luIleAspValLysTyrIleGlnProGlyValAlaSerAlaAsnGluVal 924

 3262 ATTGCGGCCGGGCGCGATGCCGTCGAAAAGACAGAAAGCGTTGCCGAACC 3311
      |||   |||   |||   |||:::||||||:::::::::::::::::
  925 IleGluAlaLysArg...AlaLeuGluLysValLysAspLeuSerAspGl 940

 3312 GGCCCGGCAGGCAGGCGGGGAAAATGTCGGCATTATGCAGGCGGAGGAAG 3361
         |||::::::   ::::::   :::|||:::      :::
  940 uGluArgGluThrLeuAlaLys...LeuGlyValSerAlaVal....... 953

 3362 AGAAAAAACGGGTGCAGGCGGATAAAGACACCGCCTTGGCGAAACAGCGC 3411
         :::   ::::::   ::::::      ::::::      |||:::
  954 .....ArgPheIleGluProAsnAsnThrIleThrValAsnThrGlnAsn 968

 3412 GAAGCGGAAACCCGGCCGGCTACC 3435
      |||      |||||||||::::::
  969 GluPheThrThrArgProSerSer 976

seq_name: /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2000.DAT:AAB01832

seq_documentation_block:
ID   AAB01832 standard; Protein; 1011 AA.
XX
AC   AAB01832;
XX
DT   11-SEP-2000  (first entry)
XX
DE   Haemophilus influenzae strain K21 HMW2A protein, SEQ ID NO:39.
XX
KW   HMW protein; hmw gene; hmwA1; hmwA2; high molecular weight;
KW   non-typeable Haemophilus influenzae; NTHi; non-encapsulated;
KW   recombinant production; Escherichia coli; antibacterial; vaccine;
KW   human disease; otitis media; epiglottitis; pneumonia; tracheobronchitis;
KW   detection; diagnosis.
XX
OS   Haemophilus influenzae strain K21.
XX
PN   WO200020609-A2.
XX
PD   13-APR-2000.
XX
PF   07-OCT-1999;   99WO-CA00938.
XX
PR   07-OCT-1998;   98US-0167568.
PR   08-DEC-1998;   98US-0206942.
XX
PA   (CONN-) CONNAUGHT LAB LTD.
XX
PI   Loosmore SM,  Yang Y,  Klein MH;
XX
DR   WPI; 2000-303789/26.
DR   N-PSDB; AAA52181.
XX
PT   Nucleic acid molecule for producing recombinant high molecular weight
PT   proteins of Haemophilus which are used as a vaccine to provide
PT   protection against Haemophilus induced diseases in humans -
XX
PS   Claim 12; Fig 21A-O; 307pp; English.
XX
CC   The invention relates to the recombinant production of Haemophilus
CC   influenzae high molecular weight (HMW) proteins in Escherichia coli. The
CC   expression construct used to effect recombinant expression comprises a
CC   promoter functional in E. coli (e.g., the T7 promoter) operably linked
CC   to a modified hmwABC operon from a non-typeable (non-encapsulated) H.
CC   influenzae (NTHi). Most HMW-expressing NTHi strains contain two hmw gene
CC   clusters termed hmw1ABC and hmw2ABC. Each hmwABC operon comprises hmwA,
CC   hmwB and hmwC genes. The hmwA genes encode the structural HMWA proteins
CC   and the hmwB and hmwC genes encode accessory proteins which are
CC   responsible for post-translational processing and secretion of the HMWA
CC   proteins. The modified hmwABC operon used in the expression construct of
CC   the invention contains an A gene modified such that it encodes only the
CC   mature HMWA. The invention also discloses hmwA genes (AAA52175-A52198)
CC   and HMWA proteins (AAB01824-B01849) from the non-typeable H. influenzae
CC   strains Joyc, K1, K21, LCDC2, PMH1, 15 and 12. The nucleic acids and
CC   vectors are used for the production of recombinant H. influenzae HMW
CC   proteins which can be used as vaccines to mediate a humoral or
CC   cell-mediated immune response to provide protection against diseases in
CC   humans caused by H. influenzae (e.g., otitis media, epiglottitis,
CC   pneumonia and tracheobronchitis). The HMW proteins are also useful as
CC   antigens in immunoassays for detecting antibodies against Haemophilus,
CC   HMW proteins and/or HMW peptides. The nucleotide sequences encoding the
CC   HMW proteins can be used to isolate and clone hmw genes from other
CC   non-typeable strains of Haemophilus via hybridisation reactions. The
CC   present sequence represents an HMWA protein from a non-typeable strain of
CC   H. influenzae.
XX
SQ   Sequence   1011 AA;


alignment_scores:
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              Ratio:  0.451                 Gaps:     54
 Percent Similarity:  49.698   Percent Identity: 20.276

alignment_block:
 US-09-303-518D-649 x AAB01832   ..

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      51 GlnLysGlyIleGluValAsnIleSerAlaThrLysAsnValThrValAs 67
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 276 TTTTCTGTGGTGTCGCGTAACGGCGTGGCGGCATTGGTGGGCGATCAAT 325
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  67 nAlaAspValAspValLysAsnGlyThrLeuValLeuHisSerGlnArgA 84

 326 ATATTGTGAGCGTGGCACATAACGGCGGCTATAACAACGTTGATTTTGGT 375
        |||::::::       ||||||:::  ||||||:::
  84 snGlyValLysIle......AsnGlyAsn.IleThrSerThrGln..... 96

 376 GCGGAAGGAAGAAATCCCGATCAACATCGTTTTACTTATAAAATTGTGAA 425
                                                     |
  97 ..................................................A 97

 426 ACGGA...ATAATTATAAAGCAGGGACTAAAGGCCATCCTTATGGCGGCG 472
     |||||    :::   ||||||   |||   |||:::   :::
  97 snGlyAsnLeuThrIleLysThrGlyGlyLysValAspValHisLysAsn 113

 473 ATTATCATATGCCGCGTTTGCATAAATTTGTCACAGATGCAGAACCTGTT 522
     |||   :::              :::|||:::::::::   :::|||:::
 114 IleThrLeuGlyMetGlyPheLeuAsnIleThrSerAspAsnAsnIle.. 129

 523 GAAATGACCAGTTATATGGATGGGCGGAAATATATCGATCAAAATAATTA 572
                 ::::::      |||   |||:::::::|||
 130 .........ThrPheGluLysGlyAspAsnLeuThrIleThr....... 140

 573 CCCTGACCGTGTTCGTATTGGGGCAGGCAGGCAATATTGGCGATCTGATG 622
                                ||||||||     |||:::
 141 .......................AlaGlnGlyAsnIle..IleSerAsnG 149

 623 AAGATGAGCCCAATAACCGCGAAAGTTCATATCATATTGCAAGTGCGTAT 672
     ::::::::   :::   |||   |||:::        :::
 149 lnGluAsnLysGlnLeuArgPheSerAsnValSerLeu............ 161

 673 TCTTGGCTCGTTGGTGGCAATACCTTTGCACAAAATGGATCAGGT..... 717
     :::   :::   :::|||   |||||||:::   |||   ::::::
 162 AsnGlyMetGlyAlaGlyLeuThrPheThrAlaAsnLysGlyAsnHisTh 178

 718 .........GGTGGCACAGTCAACTTAGGTAGTGAAAAAATT......A 751
              ||||||:::|||::::::::::::   :::       :
 178 rHisLysPheAspGlyThrLeuAsnIleSerGlyLysValValIleAsnG 195

 752 AACATAGCCCATATGGTTTTTACCAACAGGAGGCTCA............ 789
     ::   :::|||:::::::::   |||   ::::::|||
 195 lnThrThrProHisAsnIleAlaProTrpAsnAlaSerAlaAspSerTyr 211

 790 .....................TTTGGCGACAGTGGCTCACCAATGTTTAT 818
                          :::|||:::::::::::::      |||||
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 819 C......TATGATGCCCAAAAGCAAAAGTGGTTAATTAATGGGGTATTGC 862
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 228 eLysPheValAspSerAsnArgSerValAlaLeuAsnSerGlySerArgS 245

 863 AA...ACGGGCAACCCCTATATAGGAAAAAGCAATGGCTTCCAGCTGGTT 909
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 245 erPheAlaGlyValLysPheTyrGlyLysAsnAsnGluMet......... 258

 910 CGTAAAGATTGGTTCTATGATGAAATCTTTGCTGGAGATACCCATTCAGT 959
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 259 .....................LysPheAsnIleGlyAspAsnAlaAsnVa 268

 960 ATTCTACGAACCACGTCAAAATGGGAAATACTCTTTTAACGAC....... 1002
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 268 lGluPheLysLeuLysSerAsnAspAsnThrSerAsnAsnLysProLeuP 285

1003 ............................GATAATAATGGCACAGGAAAA 1023
                                  :::|||||||||   :::
 285 roIleGlnPheLeuSerAsnIleSerAlaThrGlyAsnGlyThrValSer 301

1024 ATCAATGCCAAACATGAACACAATTCTCTGCCTAATAGATTAAAAACACG 1073
     ::::::          |||   ::::|||         |||
 302 PheAspIle.........HisAlaAsnLeuSerAlaArgSerThrGluLe 315

1074 AACCGTTCAATTGTTTAATGTTTCT......................... 1098

     ::::::::|||:::|||:::|||
 315 uAsnMetSerLeuIleAsnIleSerAsnGlyValAsnPheSerIleAsnS 332

1099 ....................TTATCCGAGACAGCAAGAGAACCTGTTTAT 1128
                          |||      ::::::   :::
 332 erHisValArgGlyAsnAsnAlaPheGluIleLysLysAspLeuIleIle 348

1129 CATGCTGCAGGTGGTGTCAACAGTTATCGACCCAGACTGAATAATGGAGA 1178
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 349 AsnAlaThrGlySerAsnPheAsnLeuLysGlnThrLysAspLysPheAs 365

1179 AAATATTTCCTTTATTGACGAAGGAAAAGGCGAATTGATACTTACCAGCA 1228
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 365 pAsn............SerTyrGluLysAsnAlaIlePheSerThrHisA 378

1229 ACATCAATCAAGGTGCTGGAGGATTATATTTCCAAGGAGATTTTACGGTC 1278
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 378 snLeuThr.................IleLeuGlyGlyAsnValThrLeu 388

1279 TCGCCTGAAAATAACGAAACTTGGCAAGGCGCGGGCGTTCATATCAGTGA 1328
     :::   ||||||:::::::::            ::::::::::::|||::::::
 389 GlyGlyGluAsnSerSerSerAsnIleLysGlyAsnIleAsnIleAsnSe 405

1329 AGACAGTACCGTTACTTGGAAAGTAAACGGCGTGGCAAACGACCGCCTGT 1378
     :   ::::::||||||   :::::::::::
 405 rLysAlaAsnValThrLeuGlnAlaHisAla.................. 415

1379 CCAAAATCGGCAAAGGCACGCTGCACGTTCAAGCCAAAGGGGAA...... 1422
                   ||||||   |||::::::   |||   :::
 416 ..............GlyThrSerHisLeuAspLysLysGluArgThrLeu 427

1423 AACCAAGGCTCGATCAGCGTGGGCGACGGTACAGTCATTTTGGATCAGCA 1472
     :::   |||::::::||||||||||   :::      |||:::   ::::::
 428 ThrLeuGlyAsnValSerValGlyGlyAsnLeuAsnIleIleGlySerAs 444

1473 GGCAGACGATAAAGGCAAAAAACAAGCCTTTAGTGAAATCGGCTTGGTCA 1522
     :|||       |||   :::   :::::::::|||   :::        :
 444 nAlaHisIleAspGly...AsnLeuSerIleAlaGluSerAlaLysPheG 460

1523 GCGGCAGGGGTACGGTGCAACTGAATGCCGATAATCAGTTCAACCCCGAC 1572
     ::|||:::   :::   :::||||||         :::   |||:::
 460 lnGlyLysThrAsnAsnAsnLeuAsnIleThrGlyThrPheThr...... 474

1573 AAACTCTATTTCGGCTTTCGCGGCGGACGTTTGGATTTAAACGGGCATTC 1622
                       ::::::|||       |||:::|||
 475 ..................AsnAsnGlyThrAlaAspIleAsn........ 482

1623 GCTTTCGTTCCACCGTATTCAAAATACCGATGAAGGGGCGATGATTGTCA 1672

 482 .................................................. 482

1673 ACCACAATCAAGACAAAGAATCCACCGTTACCATTACAGGCAATAAAGAT 1722
                         |||::::::::::|||   :::   |||
 483 ..........IleLysGlnGlyValValLysLeuGlnGly......... 492

1723 ATTGCTACAACCGGCAATAACAACAGCTTGGATAGCAAAAAAGAAATTGC 1772

 492 .................................................. 492

1773 CTACAACGGTTGGTTTGGCGAGAAAGATACGACCAAAACGAACGGGCGGC 1822
                             |||   |||   :::|||||||:::|
 493 ........................AspIleThr...AsnAsnGlyAsnL 500

1823 TCAACCTTGTTTACCAGCCCGCCGCAGAAGACCGCACCCTGCTGCTTTCC 1872
     |||||:::::   :::   ::::::::::::::|||:::
 500 euAsnIleThrThrAsnAlaSerValAsnGlnLysThrIle......... 513

1873 GGCGGAACAAATTTAAACGGCAACATCACGCAAACAAACGGCAAACTGTT 1922
                :::|||||||||||||||:::   :::|||   |||
 514 ...........IleAsnGlyAsnIleThrAsnLysLysGlyAspLeuAs 526

1923 TTTCAGCGGCAGACCAACACCGCACGCCTACAATCATTTAAACGACCATT 1972
      :::::       :::   :::|||         :::::::::   :::
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 526 nIleLysAspIleLysAla...AsnAlaGluIleGlnIleGlyGlyAsnI 542

1973 GGTCGCAAAAAGAGGGCATTCCTCGCGGGGAAATCGTGTGGGACAACGAC 2022
542 leSerGlnLysGlu.....GlyAsnLeuThrIleSerSerAsp 554

2023 TGGATCAACCGCACATTTAAAGCGGAAAACTTCCAAATTAAAGGCGGACA 2072
555 LysIleAsnIleThrLysArgIleGlu..... 563

2073 GGCGGTGGTTTCCCGCAATGTTGCCAAAGTGAAAGGCGATTGGCATTTGA 2122
564 .....IleLysAlaAsp.....T 568

2123 GCAATCACGCCCAAGCAGTTTTTGGTGTCGCACCGCATCAAAGCCACACA 2172
568 hrAspGlnGlyAsnSerAspSerGlyValAlaSerAsnAlaAsnLeuThr 584

2173 ATCTGTACACGTTCGGACTGGACGGGTCTGACAAATTGTGTCGAAAAAAC 2222
585 IleLysThrLys.....GluLeuTh 591

2223 CATTACCGACGATAAAGTGATTGCTTCATTGACTAAGACCGACATCAGCG 2272
591 rLeuThrAspAsnLeuAsnIleSerGlyPheAsnLysAlaGluIleThrA 608

2273 GC......AATGTCGATCTTGCCGATCACGCTCATTTAAATCTCACAGGG 2316
608 laLysAspAsnSerAspLeu..... 614

2317 CTTGCCACACTCAACGGCAATCTTAGTGCAAATGGCGATACACGTTATAC 2366
615 .....IleIleGlyLysAlaSerSerAspAsnSerAsnAlaLysGl 628

2367 AGTCAGCCACAACGCCACCCAAAACGGCAACCTTAGCCTCGTGGGCAATG 2416
628 nIleThrPheAspLysValLysAspSerLysIleSer...AlaGlyAsnH 644

2417 CCCAAGCAACATTTAATCAAGCCACATTAAACGGCAACACATCGGCTTCG 2466
644 isAsnValThrLeuAsnSerLysValGluThrSerAsnSerAspGlySer 660

2467 ...GGCAATGCTTCA..... 2478
661 ThrGlyAsnGlySerAspAspAsnAsnIleGlyLeuThrIleSerAlaLy 677

2479 .....TTTAATCTAAGCGACCACGCCGTACAAAACGGCA 2512
677 sAspValThrValAsnSerAsnIleThrSerHisLysThrValAsnIleS 694

2513 GTCTGACGCTTTCCGGC...AACGCTAAGGCAAACGTAAGCCATTCCGCA 2559
694 erAlaSerGluGlyGlyIleThrThrLysAlaGlyThrThrIleAsnAla 710

2560 CTCAACGGTAATGTCTCCCTAGCCGATAAGGCAGTATTCCATTTTGAAAG 2609
711 ThrThrGlySerValGluValThrAlaLys..... 720

2610 CAGCCGCTTTACCGGACAAATCAGCGGC.....GGCAAGGATACGG 2650
721 .....ThrGlyAspIleSerGlyThrIleSerGlyLysThrValS 734

2651 CATTACACTTAAAAGACAGCGAATGGACGCTGCCGTCAGGCACGGAATTA 2700
734 erValThrAlaThrThrAspSerLeuThrValLysGlyGlyAlaLysIle 750

2701 GGCAATTTAAACCTTGACAACGCCACCATTACACTCAATTCCGCCTATCG 2750
751 ...AsnAlaThrGluGlyThrAlaThrLeuThrAlaSerSerGly..... 764

2751 CCACGATGCGGCAGGGGCGCAAACCGGCAGTGCGACAGATGCGCCGCGCC 2800
765 .....LysLeuThrThrGluAlaAsnSerAlaIleSerGlyAlaAsnG 779

2801 GCCGTTCGCGCCGTTCGCGCCGTTCCCTATTATCCGTTACA..... 2841
779 lyValThrAlaSerSerGlnSerGlyAspIleSerGlyThrIleSerGly 795

2842 CCGCCAACTTCGGTAGAATCCCGTTTCAACACGCTGACGGTAAACGGC.. 2889
796 LysThrValSerValThrAlaSerSerGlySerLeuThrValGlyGlyAs 812

2890 ....AAATTGAACGGT...CAGGGAACATTCCGCTTTATGTCGGAACTCT 2932
812 pAlaLysIleAsnAlaThrGluGlyAlaAlaThrLeuThrAlaThrLysG 829

2933 TCGGCTACCGCAGCGACAAATTGAAGCTGGCGGAAAGTTCCGAAGGCACT 2982
829 lyThrLeuThrThrValLysGlySerAsnIleAspAlaAsnGluGlyThr 845

2983 TACACCTTG...GCGGTCAACAATACCGGCAACGAACCTGCAAGCCTCGA 3029
846 LeuValIleAsnAlaGlnAspAlaThrLeuAsnGlyAspAlaSerGlyAs 862

3030 ACAATTGACGGTA.....GTGGAAGGAAAAGACAAC.....A 3061
862 pArgThrGluValAsnAlaValAsnAlaSerGlySerGlyAsnValThrA 879

3062 AACCGCTGTCCGAAAACCTTAATTTCACCCTGCAAAACGAACACGTCGAT 3111
879 laLysThrSerSerSerValAsnIleThrGlyAspLeuSerThrIleAsn 895

3112 GCCGGCGCGTGGCGTTACCAACTCATCCGCAAAGACGGCGAGTTCCGCCT 3161
896 Gly.....LeuAsnIleIleSerLysAsnGlyLys..... 905

3162 GCATAATCCGGTCAAAGAACAAGAGCTTTCCGACAAACTCGGCAAGGCAG 3211
906 ....AsnThrVal.....ValLeuLysGlyAlaG 914

3212 AAGCCAAAAAACAGGCGGAAAAAGACAACGCGCAAAGCCTTGACGCGCTG 3261
914 luIleAspValLysTyrIleGlnProGlyValAlaSerAlaAsnGluVal 930

3262 ATTGCGGCCGGGCGCGATGCCGTCGAAAAGACAGAAAGCGTTGCCGAACC 3311
931 IleGluAlaLysArg...AlaLeuGluLysValLysAspLeuSerAspGl 946

3312 GGCCCGGCAGGCAGGCGGGGAAAATGTCGGCATTATGCAGGCGGAGGAAG 3361
946 uGluArgGluThrLeuAlaLys...LeuGlyValSerAlaVal..... 959

3362 AGAAAAAACGGGTGCAGGCGGATAAAGACACCGCCTTGGCGAAACAGCGC 3411
960 .....ArgPheIleGluProAsnAsnThrIleThrValAsnThrGlnAsn 974

3412 GAAGCGGAAACCCGGCCGGCTACC 3435
975 GluPheThrThrArgProSerSer 982
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